LEARNING TO PLACE ONE FOOT IN FRONT OF THE OTHER: INVESTIGATION OF ACTION AND PERCEPTION IN HUMAN SPLIT-BELT WALKING

by

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Abstract

Walking must be highly adaptable to new environments - people quickly learn new calibrations of their walking pattern to account for ice, sand, or even high heels. Unfortunately, gait dysfunction results from many types of neurological insult or injury. Recently, it has been suggested that we may be able to leverage the adaptability of the human nervous system to improve gait rehabilitation. One method for inducing locomotor learning is to have subjects walk on a split-belt treadmill (a treadmill with one belt for each foot). When one treadmill belt is driven faster than the other, subjects are forced to adapt their gait pattern to compensate for this perturbation. These newly learned gait patterns are then retained when the belts are returned to equivalent speeds. However, we still know very little about how the locomotor system adapts and stores new gait patterns. Therefore, the focus of this doctoral research was to investigate how the human nervous system adapts to walking in new environments in order to build a foundation for improving gait rehabilitation. First, we developed a model for split-belt walking that demonstrated that subjects were learning where to place their feet relative to their body during this locomotor learning experience.

ABSTRACT

We applied this model to split-belt walking as well as a condition in which subjects marched in place with one foot on a stationary surface and walked with the other foot on a moving surface. Second, we examined the effect of simultaneously utilizing an explicit strategy while adapting to split-belt walking. Results demonstrated that the explicit strategy neither enhanced nor interfered with the after-effects of split-belt adaptation. Finally, we investigated how one's subjective speed perception was altered during split-belt walking. We discovered that the perceptual recalibration could be predicted simply based on how subjects were walking in the split condition. Overall, these results advance neuroscience principles of human locomotor learning.

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Dedication

To my wife Adrienne: my love, my life, my friend.

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Chapter 1

Introduction

> *Science is about what is, engineering is about what can be.*
> Neil Armstrong

Walking is the primary form of locomotion for most people. In order to properly perform this action, our nervous system must simultaneously control and coordinate approximately 80 billion neurons, 640 muscles and 206 bones. Yet, we are able to accomplish this with little to no conscious effort, allowing us to pay attention to other tasks. For instance, we are able to successfully walk down a hallway while at the same time talking to friends and looking at our phones.

A person's walking ability is an important part of mobility, independence and community involvement. It has been shown that walking performance in elderly people is a strong prognostic for quality of life (Bowling, 1995), morbidity (Newman et al., 2003) and mortality (Newman et al., 2006; Studenski et al., 2011). Unfortunately, gait dysfunction results from many types of neurological insult or injury. For

example, patients who experience a cerebral stroke tend to take unequal step lengths, patients with Parkinsons tend to take slow small steps, and patients with cerebellar damage tend to have unsteady and uncoordinated gaits. In order to understand the causes of each gait dysfunction, it is important for us to investigate walking in neurologically healthy people so that we can develop a better foundation of normal walking characteristics. With this knowledge, we will be able to properly identify gait dysfunction as well as to design better rehabilitation strategies.

Exoskeletons, prosthetics and autonomous walking robots are all great examples of ways in which engineers are attempting to replicate or apply our knowledge of normal human walking. While design of these machines has made great progress over the last several decades, in general these machines are limited to movement on flat smooth terrain. This is due to the fact that engineers are generally designing control algorithms that result in a small set of well-defined gait patterns.

On the other hand, the human nervous system is constantly altering our walking pattern when encountering new environments and new situations. For example, as compared to normal pavement walking, people tend to walk slower with a wider base of support while walking on ice; whereas people push off with more force when walking over sand (Lejeune et al., 1998). Furthermore, people modify their walking pattern with changes in footwear (e.g. walking in high heels is drastically different than walking barefoot). Our walking pattern is also altered over longer time scales as our body changes sizes due to age and weight changes. All of these examples indicate

that the nervous system (and any artificial control system) must be highly flexible and capable of adapting to new circumstances.

The focus of this dissertation is to investigate how the healthy human nervous system learns to walk in new environments. This work is important on a general level, because it advances basic neuroscience principles in motor learning as they apply to human locomotion. This work is important on an engineering level, because the observed principles may be applicable for improving design and control of exoskeletons, prosthetics and autonomous walking robots. Finally, this work is important on a clinical level, because it will help inform how to better design rehabilitation strategies for patients with gait dysfunction.

1.1 Introduction to human walking

Walking is a complex form of locomotion that requires rhythmic control of multiple muscles and joints. With many advances in motion capture and recording systems, the kinematics and kinetics of normal human locomotion have been extensively studied (Rose et al., 2006). Although we can quantify *how* we walk, the question still remains on *why* we walk the way we do.

Given that walking is a cyclic motion, researchers decompose walking into discrete strides, which are defined as the time between heel strike on one leg to the next heel strike on the same leg. A single stride consists of stance and swing phases on each

side of the body. Stance phase (approximately 60% of the stride cycle) begins with heel strike on the ground and ends when that foot leaves the ground. Conversely, swing phase (approximately 40% of the stride cycle) begins when the foot leaves the ground and ends at heel strike of that same foot. The stance phases for the two limbs partially overlap during walking such that both limbs are on the ground at the same time (i.e. double support). As walking speed increases, the double support times decrease until the person is running with no double support time. In general, the stride cycles of the two limbs are in anti-phase such that gait events (e.g. heel strike) on one limb occur half way through the stride cycle of the other limb. The time between heel strikes of opposite limbs is referred to as step time, which in normal symmetric walking means that one step time is half of one stride time.

In this dissertation, we also focus on spatial parameters such as foot placement, step length and stride length. We define foot placement as the anterior-posterior distance from the body to the ankle at heel strike, step length as the anterior-posterior distance between the two ankles at heel strike and stride length as the distance traveled between heel strike and toe-off on the same leg. Here, we will analyze both spatial and temporal parameters on a stride-by-stride basis so that we are able to observe how people modify these parameters as they walk in new environments.

1.2 Introduction to motor adaptation

Learning new movement patterns is known as motor learning (Schmidt and Lee, 1988). Motor learning can be separated into skill learning and motor adaptation. In skill learning, people learn a new skill such as swinging a golf club, riding a bicycle or playing a musical instrument by learning a novel pattern of muscle activation (Krakauer, 2009). This type of learning is generally permanent as one never really forgets how to ride a bicycle. On the other hand, in motor adaptation, people modify existing motor patterns to new environments or situations (Krakauer, 2009). For example, when people put on a new pair of glasses, their nervous system slightly alters the oculomotor muscle activation to reestablish accurate and clear vision. When the glasses are removed, the nervous system reverts back to the original muscle activation pattern. Hence, motor adaptation is a more temporary form of learning. In this dissertation, we will focus on how people learn to walk in novel locomotor environments, which falls under the realm of motor adaptation since all individuals know how to walk prior to the experiments and are only slightly modifying their walking patterns.

In the laboratory, motor adaptation is studied by presenting a novel environment and observing how subjects adapt to this new situation. These experiments typically consist of a baseline phase, a learning phase (i.e. adaptation) and a post-learning phase (i.e. post-adaptation). During the baseline phase, the baseline motor behavior of subjects is recorded in an environment. During the learning phase, a perturbation is introduced to the environment, requiring subjects to adapt their motor behavior. Fi-

nally, during the post-learning phase, the perturbation is removed and after-effects are observed that gradually return to baseline behavior. These after-effects are thought to reveal what the nervous system learned during the learning phase (Shadmehr and Mussa-Ivaldi, 1994; Weiner et al., 1983).

For example, throwing with prisms is a well-studied motor learning paradigm (Martin et al., 1996). In these experiments, subjects begin by accurately throwing balls at a target. Eventually, subjects put on a pair of prism glasses that laterally shift the subjects vision to one side. Initially, subjects throw straight along the visual field which due to the prism glasses results in a large error on the target. Through trial-and-error practice, subjects learn to adjust their throwing and hit the target by accounting for the lateral visual shift. When the prism glasses are removed, subjects exhibit an after-effect in the opposite throwing direction of the prism shift, indicating that they had learned to throw to counter the prism. Similar patterns of motor adaptation have been also observed in upper-limb reaching for force-fields (velocity-dependent perturbations tangential to movement direction, Shadmehr and Mussa-Ivaldi, 1994) and visuomotor rotations (perturbations that rotate a cursors movement direction on a screen, Krakauer, 2009; Krakauer et al., 2005).

Why do subjects adapt and show after-effects? One theory suggests that the nervous system builds an internal model of how the body should move in an environment (Wolpert et al., 1995). The internal model can be used to predict future states of the body for a given motor command. Since sensory feedback generally is too slow to

be useful for rapid movement, the internal model can be used to make quick adjustments to the motor command when the predicted state is different than the desired state. The internal model can also be useful for predicting the sensory consequences of the motor command. Differences between the predicted and actual sensory feedback are referred to as sensory prediction errors. It has been proposed that these sensory prediction errors are used to update the internal model (i.e. adaptation) as well as to update the motor command (Wolpert et al., 1995). Therefore, it appears that subjects adapt to new environments by updating their internal model. Thus, the after-effects represent how the updated internal model is expressed in the original unperturbed environment.

1.3 Locomotor learning with a split-belt treadmill

In this dissertation, we induce locomotor learning by having subjects walk on a split-belt treadmill, a treadmill with one belt for each foot. When one belt is driven faster than the other, healthy subjects adapt their walking pattern over a short period of time to this new walking environment. This newly learned walking pattern is then retained for a brief period of time when the treadmill belts are returned to the same speed (Vasudevan and Bastian, 2010). Similar locomotor learning has also been shown previously with a swing resistance robotic orthosis (Lam et al., 2006) and a circular

treadmill (Gordon et al., 1995; Weber et al., 1998).

The first use of split-belt walking in humans began in 1987 with 7 month old infants (Thelen et al., 1987). While these infants were not capable of normal walking on their own, these infants when supported demonstrated well-coordinated stepping motion on a split-belt treadmill when the belts moved the same speed as well as different speeds (Thelen et al., 1987). In infants, the corticospinal tract is still developing, so it is likely that this stepping behavior is controlled by lower-level neural networks such as the spinal cord. A similar stepping behavior was also shown previously in decerebrate cats (Forssberg et al., 1980). This work suggests that locomotion may be controlled by the spinal cord with a central pattern generator (CPG), which is defined as a neural network capable of generating rhythmic motion without descending input or sensory feedback. Additional work in both cats (Andersson and Grillner, 1981, 1983; Duysens et al., 2000; Duysens and Pearson, 1976, 1980; Grillner and Rossignol, 1978; McVea et al., 2005) and infants (Pang and Yang, 2000; Yang et al., 2004, 2005) has suggested that sensory feedback such as hip extension and limb loading can modify the gait cycle while maintaining coordination between the two limbs. However, it appears that as myelination increases in early human infancy the supraspinal networks play a more dominate role in locomotion control, since there has been very little evidence of CPGs in human adults with spinal cord transections (Calancie et al., 1994; Dimitrijevic et al., 1998).

Nevertheless, non-infant human studies with split-belt treadmills began in 1994

(Dietz et al., 1994). The initial studies focused on the temporal aspects of locomotion and revealed that subjects quickly adapted (within 20 strides) to the split-belt condition by shortening the stance phase and lengthening the swing phase on the fast limb and vis versa on the slow limb (Dietz et al., 1994; Prokop et al., 1995). Additional experiments revealed that these temporal changes scaled with belt speed differences (Zijlstra and Dietz, 1995). This initial work suggests that temporal aspects of walking adapt quickly and are important for maintaining appropriate gait cycles across different belt speed combinations.

In the seminal work by Reisman and colleagues, the adaptation and storage of both temporal and spatial parameters were investigated (Reisman et al., 2005). They observed that intralimb parameters such as stride length and percent stance time were reactive parameters that changed quickly with new belt speed differences and showed no after-effects when the belts were returned to the same speed. On the other hand, Reisman and colleagues observed that interlimb parameters such as step length and percent double support time incrementally adapted over hundreds of strides and showed robust after-effects. More recent work has demonstrated that the interlimb parameters are dissociable with temporal parameters adapting faster than spatial parameters (Malone et al., 2012). Similar observations for intralimb and interlimb parameters have also been seen when one belt is moving in the opposite direction (Choi and Bastian, 2007). Additional work has revealed that these after-effects vary with walking speed with the largest occurring at the slowest training speed (Vasude-

van and Bastian, 2010). However, these after-effects appear to be walking specific as they do not carry over to running (Ogawa et al., 2015a,b, 2012). As a result, it appears that locomotor learning on the split-belt treadmill involves both temporal and spatial adaptation, but only the interlimb components exhibit after-effects in walking.

What drives locomotor adaptation? There is evidence to suggest that human walking parameters are optimized to minimize energetic cost (Zarrugh et al., 1974). While split-belt walking appears to be more costly than regular walking (Roper et al., 2013), it has been shown that changes in metabolic cost during adaptation occur on a similar time-scale to adaptation of step length symmetry (Finley et al., 2013). This indicates that step length symmetry can be considered an error signal that drives learning. Initially, step length symmetry exhibits large error when the belts are abruptly split but become more symmetric during adaptation. When the belts are tied to the same speed, subjects show after-effects (i.e. errors) in the opposite direction, a common sign of motor learning. While step length symmetry may represent an error signal, it is still unknown what parameters are being updated with this error signal. These output parameters would gradually change during adaptation, persist at the beginning of post-adaptation and then gradually return to the baseline. If we are able to identify these output parameters for split-belt walking, we will have a better understanding of what gait characteristics can be targeted with split-belt walking with rehabilitation.

1.4 Generalization of motor learning

In order for studies of motor learning to be applicable to rehabilitation, the observed after-effects have to transfer to real-world movements. This idea is known as generalization in which learning in one context transfers to other contexts (Schmidt and Lee, 1988). Generalization of motor learning of upper limb movements has been studied extensively for force-field reaching (Shadmehr, 2004; Shadmehr and Mussa-Ivaldi, 1994), visuomotor rotation (Krakauer et al., 2006), and prism adaptation (Morton and Bastian, 2004; Savin and Morton, 2008). Likewise, robust generalization to overground walking has been observed for a variety of locomotor experiments including jogging in place on a regular treadmill (Anstis, 1995), stepping in place on a circular treadmill (Earhart et al., 2002; Weber et al., 1998) and walking on a split-belt treadmill (Huynh et al., 2014; Mukherjee et al., 2015; Reisman et al., 2009; Torres-Oviedo and Bastian, 2010, 2012). In split-belt walking, subjects adapt to walking on the split-belt treadmill and then immediately limp when walking overground. Alteration of sensory cues such as walking with eyes closed (Torres-Oviedo and Bastian, 2010) or tactile vibration (Mukherjee et al., 2015) can increase the amount of transfer. Another method for increasing transfer is to introduce a perturbation gradually instead of abruptly because in this manner subjects tend to assign movement errors to themselves instead of the environment (Berniker and Kording, 2008; Torres-Oviedo and Bastian, 2012). Therefore, sensory cues and the similarity of movement patterns in the two contexts likely play a large role in the amount of transfer between con-

texts (Shadmehr, 2004). As a result, rehabilitation strategies should be designed in a manner that most closely resembles real-world environments and contexts.

1.5 Explicit and implicit components of motor learning

Motor learning utilizes a suite of learning mechanisms including both explicit and implicit processes. For example, when people are stepping on stones to cross a stream they are explicitly thinking about changes to their walking pattern, but when they are walking on sand their nervous system implicitly alters their walking pattern. Adaptive learning on the split-belt treadmill can be considered mostly implicit as people do not consciously think about how they are walking and are surprised by the after-effects when the belts are returned to the same speed. Nevertheless, people are able to follow instructions during experiments. Recently, Malone and Bastian instructed subjects to equalize their step lengths during an abrupt split-belt perturbation (Malone and Bastian, 2010). They observed that subjects tended to adapt faster with instruction as compared to controls but had no difference in post-adaptation. However, prior work in a reaching paradigm has shown that the rate of learning can influence the rate of deadaptation (Huang and Shadmehr, 2009), so further work with a controlled rate of learning is needed to investigate the effects of explicit instruction on after-effects. This is critical for rehabilitation as physical therapists tend to tell patients

exactly what to do during training.

1.6 Sensory perception during motor learning

In order for the nervous system to be able to adapt to new circumstances, it needs to be able to detect or sense errors. These sensed errors can occur because the body moved incorrectly or because the nervous system did not sense the world accurately. Interestingly, after subjects walk on the split-belt treadmill, they report that the previously slow belt is now faster when the belts are returned to the same speed (Hoogkamer et al., 2015a; Jensen et al., 1998; Lauzière et al., 2014; Reisman et al., 2005, 2009; Vazquez et al., 2015). Similar perceptual after-effects as measured through localization tasks have been observed following force-field reaching (Brown et al., 2007; Haith et al., 2009; Ostry et al., 2010) and visumotor reaching (Cressman and Henriques, 2009; Malfait et al., 2008; Simani et al., 2007; van Beers et al., 2002). Therefore, it appears that adaptation induces both perceptual learning and motor learning. In this dissertation, we investigate a method for quantifying the perceptual learning in split-belt walking as well as a theory for connecting it to the motor learning.

1.7 Neural correlates of motor learning

Many areas of the central nervous system are likely involved during the motor learning process. From studying multiple patient populations with targeted deficits we are able to observe which areas are important. While this dissertation focuses on healthy individuals, insights from patients with neurological damage must be considered when designing new adaptive learning paradigms.

Insights from cerebellar damage

The cerebellum has long been considered important for error-based motor learning (Albus, 1971; Marr, 1969; Thach et al., 1992). While a thorough discussion of the cellular components of the cerebellum is beyond the scope of this thesis (for a review see Taylor and Ivry, 2014), we will briefly cover behavioral experiments with patients with cerebellar degeneration. These patients have shown deficits in learning in a wide variety of experiments including split-belt walking (Morton and Bastian, 2006; Vasudevan et al., 2011), throwing with prisms (Martin et al., 1996), reaching with prisms (Weiner et al., 1983), anticipatory catching (Lang and Bastian, 1999), postural standing (Horak and Diener, 1994), and force-field reaching (Gibo et al., 2013; Smith and Shadmehr, 2005). Morton and Bastian had patients with severe cerebellar damage walk on the split-belt treadmill with the belts moving different speeds in an abrupt manner. They observed that the patients were capable of modifying the reac-

tive locomotor parameters (stride length and percent stance) but did not modify the adaptive parameters (step length and percent double support). Since patients did not adapt during learning, they also showed no after-effects. Note that recent work with patients with focal cerebellar damage did not show these deficits (Hoogkamer et al., 2015b), suggesting that the whole cerebellum is an important component of adaptive learning with the split-belt treadmill. This is further supported by evidence that there are neurophysiological changes in the cerebellum in healthy individuals following split-belt adaptation (Jayaram et al., 2011) and that transcranial direct current stimulation over the cerebellum can alter rates of adaptation (Jayaram et al., 2012). Adaptation impairments have also been observed with patients who have suffered tramatic brain injury, suggesting possible damage to cerebellar or brainstem networks (Vasudevan et al., 2014). As a result, it is unlikely that the split-belt treadmill can be used for rehabilitation of patients with cerebellar damage.

Insights from cerebral stroke

Stroke is a leading cause of disability in America with most strokes occurring in the cerebral cortex (Go et al., 2014). A major goal of these patients is to regain the ability to walk (Lord et al., 2004; Lord and Rochester, 2005; Mayo et al., 1999). While many patients are able to relearn to walk (Lord et al., 2004; Lord and Rochester, 2005; Petrilli et al., 2002), many continue to have difficulty walking even after extensive rehabilitation (Ada et al., 2003; Bowden et al., 2006; Chen et al., 2005; Hsu et al.,

2003; Lamontagne and Fung, 2004; Nadeau et al., 1999; Olney et al., 1994; Olney and Richards, 1996). Step length asymmetry is a common hallmark of patients with cerebral stroke (Hsu et al., 2003; Lamontagne and Fung, 2004; Olney et al., 1994), suggesting that correcting this problem should be a focus for rehabilitation (Kahn and Hornby, 2009). Therefore, the split-belt treadmill potentially could be a useful rehabilitation tool as it targets improvements of step lengths (Reisman et al., 2005).

Reisman and colleagues first tested patients with cerebral stroke on the split-belt treadmill in 2007 (Reisman et al., 2007). They demonstrated that patients with cerebral stroke were able to modify both reactive and adaptive parameters to the split-belt treadmill and showed after-effects in step length difference when the belts were returned to the same speed. These after-effects produced more symmetric walking for these patients when their baseline asymmetries were initially exaggerated during training. On the other hand, if the baseline asymmetries were initially reduced during training, the after-effects were worse (i.e. larger asymmetry after learning). Similar work in reaching with augmented feedback has shown that the greatest improvements are associated with exaggerated errors (Patton et al., 2006; Reinkensmeyer and Patton, 2009). Further work has shown that while stroke patients learn slower, they are able to have the same after-effects as controls if given enough training time (Malone and Bastian, 2014; Tyrell et al., 2014). While the initial locomotor experiment consisted of a short training period entirely on the treadmill, additional work has revealed that repetitive locomotor training potentially can produce lasting changes for

months (Reisman et al., 2010, 2013). Recently, Wutzke and colleagues showed that patients were unability to perceive their own spatiotemporal asymmetries, suggesting that the perceptual learning aspect of split-belt walking may also be beneficial to patients (Wutzke et al., 2015). Overall, these locomotor studies are important as they demonstrate that adaptive learning on the split-belt treadmill may be a fruitful route for rehabilitation for patients with cerebral stroke.

Insights from hemispherectomy

The studies above revealed that the cerebellum is important for adaptive locomotor learning and that focal cerebral strokes do not interfere with the reactive or adaptive components. Therefore, this raises the question if the cerebral cortex is required for human locomotor learning. Children with hemispherectomy surgery (removal of one cerebral hemisphere) were tested on the split-belt treadmill and results revealed that reactive components and spatial adaptive components were intact but temporal adaptive components were impaired (Choi et al., 2009). This suggests that reactive parameters may be controlled in the brainstem or spinal cord, whereas the adaptive components involve both the cerebellum and cerebral cortex. It is likely that the cerebellum is involved with the spatial adaptive parameters since prior work with brain stimulation over the healthy cerebellum was able to alter learning spatial parameters but not temporal parameters (Jayaram et al., 2012).

Insights from Parkinsons disease

Another population that has been studied with the split-belt treadmill is patients with Parkinsons disease (PD). Initial studies focusing on the temporal aspects for short adaptation periods revealed that patients with PD had difficulty altering the stride frequencies and percent stance time for a range of belt speed differences (Dietz et al., 1995). Further work showed that only patients with PD who exhibited freezing of gait had difficulty with timing but those who were non-freezers had no difficulty (Mohammadi et al., 2015; Nanhoe-Mahabier et al., 2013). Recent studies by Roemmich and colleagues investigated step length adaptation for longer adaptation periods (Roemmich et al., 2014a,b). They showed that patients with PD had no difficulty in early adaptation compared to controls but were impaired during late adaptation, resulting in larger step length asymmetries in late adaptation (Roemmich et al., 2014b). They also demonstrated that removal of dopaminergic medication impaired the aftereffects but not the ability to learn (Roemmich et al., 2014a). Similar results were also observed for prism reaching with patients with PD (Stern et al., 1988). This suggests that dopaminergic pathways may be involved with retention of learning but that other pathways (i.e. cerebellar) are involved with the acquisition. This provides a possible explanation for why cerebellar brain stimulation affects the rate of learning but not the retention (Jayaram et al., 2012). Given that dopaminergic pathways are involved with reward and reinforcement, it is possible that some type of reinforcement must be considered when designing rehabilitation strategies for lasting impact.

Insights from aging

Multiple studies have investigated the differences in adaptation on the split-belt treadmill for a range of ages, since the nervous system changes as the body ages. Children less than six years old are able to adapt temporally to the split-belt treadmill but are unable to learn the spatial pattern (Musselman et al., 2011; Vasudevan et al., 2011). Other work has demonstrated that older subjects (greater than 70 years old) adapt less and more slowly to the split-belt treadmill (Bruijn et al., 2012). These older subjects tended to have more impairment in the spatial domain than the temporal domain. Given these results, it is likely that the cortico-cerebellar pathways are still developing in younger children but are degrading with age. As a result, when designing rehabilitation strategies, physical therapists must also consider the age of the individual.

1.8 Scope of this dissertation

This doctoral research advances the understanding of basic neuroscience principles in motor learning as they apply to human locomotion. We have demonstrated that (1) adaptive learning can occur on a single belt treadmill, (2) adaptive learning acts independently of explicit strategy and (3) adaptive learning also alters how one perceives the world through sensory-cancellation.

Aim 1: Adaptive learning can occur on a single belt treadmill. Split-

belt treadmills are expensive (approximately $100,000) and are not universally available for rehabilitation; therefore, there exists a need for an effective walking adaptation protocol that could be performed using a common single-belt treadmill. In this project, we asked if gait adaptation occurs while a person walks in place with one leg (i.e. marches) on a stationary surface while walking with the other leg on a single moving treadmill belt. Results indicated that this marching-walking hybrid induced adaptation that was similar to split-belt walking. These findings suggest that physical rehabilitation with this marching-walking hybrid paradigm on conventional treadmills may produce gait changes comparable to what is observed during split-belt training. This new technique therefore represents a novel cost-effective and accessible rehabilitation strategy for improving gait. This chapter has been published previously in the Journal of Neurophysiology (Long et al., 2015).

Aim 2: Adaptive learning acts independently of explicit strategy. The ability to learn a new walking pattern through rehabilitation depends on a suite of learning mechanisms including instructive and adaptive learning. In instructive learning, patients are explicitly told how to move (typical of classic rehabilitation strategies). In adaptive learning (such as with the split-belt treadmill), a patient's movements are perturbed and the patient must adapt and recalibrate to these perturbations to successfully move. However, little is known about how these two learning mechanisms interact. Therefore, the second component of my dissertation investigated how to optimally combine adaptive learning and explicit strategies to make

lasting changes in gait patterns. We used a custom-designed biofeedback display to instruct subjects where to step while they simultaneously adapted walking on the split-belt treadmill. Specifically, we investigated whether adaptive learning was affected by using instruction to make split-belt treadmill walking easier or more difficult. We demonstrated that using an explicit strategy to make split-belt walking more difficult did not inhibit learning a new gait pattern; in fact, subjects learned the new gait pattern as if there was no instruction at all. Similarly, when instruction was used to make split-belt walking easier, adaptive learning was unaffected by the instruction. These experiments demonstrate that in walking, explicit strategy and adaptive learning act independently. This is a very important result for gait rehabilitation, as it challenges the status quo of rehabilitation by suggesting that instructing patients how to move does not necessarily improve rehabilitation outcomes in all settings.

Aim 3: Adaptive learning alters how one perceives the world through sensory-cancellation. Consider what happens when you step onto an icy walkway-you must accurately perceive the environment and then use this information to adapt your walking to stay upright. In this third project, we show that adaptive learning on the split-belt treadmill changes both motor and perceptual calibrations during walking, and that these strong perceptual changes can be explained by sensory-cancellation (where expected sensory consequences of an action are cancelled from the incoming sensory signal). Prior to exposure to split-belt walking, subjects do not expect the belt speeds to differ. However while walking in a split-belt condition,

healthy subjects develop an expectation that one belt will be moving faster than the other. When the belts are then returned to the same speed, subjects express both a motor after-effect (unequal foot placements) and a perceptual after-effect (reporting that the previously slow belt is now faster). We hypothesized that this perceptual after-effect is caused by the continued expectation of different belt speeds cancelling a portion of the incoming sensory signal. To evaluate this sensory-cancellation hypothesis, we designed a multi-phase experiment to measure speed perception and to estimate subjects' speed expectations. We then used the speed expectations to predict the subjective perception based on sensory-cancellation and compared these predictions to the actual measurements. These results provide clear evidence that a sensory-cancellation mechanism can explain the perceptual after-effect observed during locomotor learning, suggesting that perceptual and motor learning both depend on your expectations of the environment. These findings provide significant insight into how the human sensorimotor system operates during locomotion.

Chapter 2

A marching-walking hybrid induces step length adaptation and transfers to natural walking

Walking must be highly adaptable to new environments in order to be useful — people quickly learn new calibrations of their walking pattern to account for ice, sand, or even high heels. One novel environment used for studying human walking adaptation is the split-belt treadmill which has two belts that can move at different speeds (Reisman et al., 2005). During split-belt adaptation where one treadmill belt moves faster than the other, people initially walk with a limp (unequal step lengths) and adapt over hundreds of strides to equalize their step lengths. When the treadmill belts are returned to the same speed, they limp in the opposite direction, indicating

that they stored a new walking pattern, and this pattern must be actively de-adapted (Reisman et al., 2005).

Split-belt adaptation leads to changes in the movement of both legs to re-establish step length symmetry (Choi and Bastian, 2007; Reisman et al., 2005). Recently, it has been shown that step length symmetry can be decomposed into spatial (i.e. where to step), temporal (i.e. when to step) and perturbation contributions (Finley et al., 2015). In split-belt walking, the perturbation term is a result of the belts moving at different speeds. To walk with symmetric step lengths, the spatial and temporal terms must adapt to counteract this perturbation.

Here we asked whether spatial and temporal adaptation can occur if a person walks in place with one leg (i.e. marches) on a stationary treadmill belt while walking with the other leg on a moving belt (i.e. marching-walking hybrid). This marching-walking hybrid pattern is interesting for several reasons. First, it allows us to determine if unilateral alteration of some of the sensory information known to be important in walking (e.g. stretch of the hip flexors, limb loading and body weight transfer) (Andersson and Grillner, 1981, 1983; Duysens and Pearson, 1980; Grillner and Rossignol, 1978; Pang and Yang, 2000) modulates the process of adaptation. For example, it is possible that adaptation might be disrupted with the decrease of some of these essential sensory cues. Second, the marching-walking hybrid hypothetically should not allow the leg on the stationary belt to dramatically change its stepping location. Thus, it could reduce the availability of the spatial learning strategy in adapting leg

motions towards symmetry.

Third, this type of locomotion is similar to previous research in a reduced gait. In a reduced gait, one limb is walking on a moving surface while the other limb steps in place and is required to remain "stiff" to reduce joint movement (Faist et al., 1999; Van de Crommert et al., 1996). Reflex and EMG analysis of the reduced gait indicated that there were similar patterns of phase dependent modulation in the lower limbs (Faist et al., 1999; Van de Crommert et al., 1996). This suggests that the marching-walking hybrid may partially activate overlapping neural adaptation circuits to that of split-belt walking.

Finally, understanding if adaptation can occur in a marching-walking hybrid condition might have clinical implications for individuals who have suffered a stroke and walk with asymmetric step lengths (Allen et al., 2011; Balasubramanian et al., 2007; Hall et al., 2012; Patterson et al., 2010). We have previously shown that stroke survivors can learn to correct their step length asymmetry from long-term training on a split-belt treadmill (Reisman et al., 2013). However, split-belt treadmills are generally expensive and are not universally available for rehabilitation. Therefore, it would be important to know if they could benefit from adaptation with the marching-walking hybrid as rehabilitation could be completed on a single-belt treadmill.

A couple of studies have assessed if unilateral stepping affects over ground walking — one study showed that it transfers to over ground walking much less than split-belt walking in controls (Huynh et al., 2014) and another study showed it produces

modest over ground changes following long-term training in stroke survivors (Kahn and Hornby, 2009). However, in unilateral stepping one foot remains on the ground the entire time and the other steps on and off a moving surface (similar to a pattern that would be used to propel a skateboard). We hypothesize that a pattern that more closely matches normal walking with alternating single limb supports, such as a walking-marching hybrid, might lead to greater adaptive changes in walking.

Here we tested if a marching-walking hybrid pattern can induce adaptation and de-adaptation similar to split-belt walking. We then asked if the adapted marching-hybrid pattern would transfer to more natural, over ground walking in a similar way as results from split-belt adaptation. Furthermore, we are interested in understanding how the nervous system solves this spatial-temporal balance compared to that of the split-belt walking. The results presented here are important for expanding our understanding of locomotor adaptation, which potentially could be beneficial for walking rehabilitation.

2.1 Methods

Subjects

57 healthy naive subjects (31 male, 23.6 ± 0.65 years old) participated in this study. The Johns Hopkins Institutional Review Board approved all protocols and all subjects gave informed written consent before participating.

Data collection

Infrared-emitting markers were placed bilaterally on each subject's body over the fifth metatarsal head, lateral malleolus, lateral femoral epicondyle, greater trochanter, iliac crest and acromion process as shown in the first image of Figure 2.1A. During treadmill (Woodway Split-Belt treadmill) walking, the 3-D position of the markers was recorded at 100 Hz with an Optotrak (Northern Digital) motion capture system. Vertical ground reaction forces were collected at 1000 Hz from the force plate under each belt while the subjects were on the treadmill and these forces were synchronized with the kinematic data. These forces were used to compute heel-strike and toe-off events, and were not otherwise included in our analysis. For the over ground portions of the walking experiment, the time and location of heel strike were recorded using a Zeno Walkway (ProtoKinetics, Havertown, PA) of 6 meters in length. The over ground walking was recorded in a different area of the lab, and Optotrak markers were not recorded during those portions of the experiment.

Overall protocol

Subjects walked on the split-belt treadmill with one foot on each belt. The treadmill belt speeds were independently controlled with custom software (Vizard, WorldViz). Sometimes the treadmill belts moved at the same speed ("tied belts") and sometimes they moved at different speeds ("split belts"). During split-belt walking,

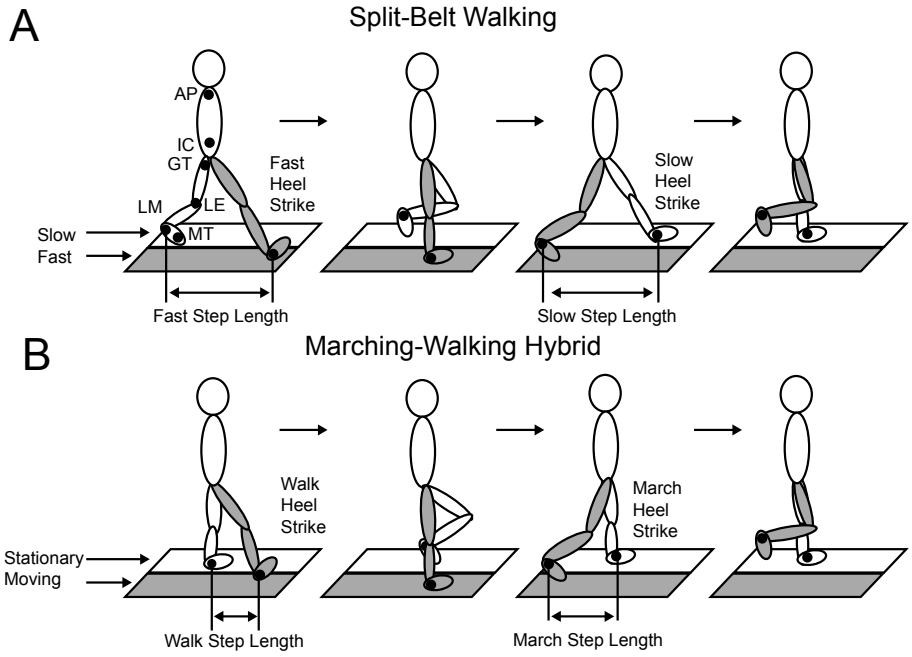

Figure 2.1: Illustrations of step length and marker positions for (**A**) split-belt walking and (**B**) the marching-walking hybrid. Step length is defined as the anterior-posterior distance between the ankle markers at heel strike. Fast (walk) step length occurs at heel strike on the fast (walk) belt and slow (march) step length occurs at heel strike on the slow (march) belt. Infrared emitting markers were placed bilaterally on the fifth metatarsal head (MT), lateral malleolus (LM), lateral femoral epicondyle (LE), greater trochanter (GT), iliac crest (IC) and acromion process (AP).

the faster belt was always under the right foot. A thin divider was placed between the belts to prevent them from stepping on the opposite belt. Subjects wore a non-weight bearing safety harness attached to the ceiling. They were given instructions to hold on to the treadmill's handrail when the belts started moving and then let go and cross their arms within the first few seconds. Near the end of each trial they were instructed to hold on to the handrail before the belts stopped moving. While they were walking, subjects were told to not look at their feet and watch a self-selected movie or show on a TV screen placed in front of them.

In *Experiment 1*, 29 subjects (16 male, 22.8 ± 0.9 years old) completed the protocol shown in Figure 2.2 to assess differences between a marching-walking hybrid and split-belt training. The subjects were randomly divided into two groups. The SPLIT_TM group (n = 15) performed a standard split-belt experiment (Figure 2.2A) with the slow belt moving at 0.5 m/s and the fast belt moving at 1.5 m/s. This type of walking can be seen in Figure 2.1A. The MARCH_TM group (n = 14) performed the protocol in Figure 2.2B with the marching-walking hybrid discussed above: the slow belt was stationary and the fast belt moved at 1.0 m/s. The marching-walking hybrid can be seen in Figure 2.1B. Note that all belt speeds at 0 m/s are marching. Thus, the difference in belt speeds (fast-slow) was 1.0 m/s for both groups. During adaptation, the subjects in the MARCH_TM group were instructed to march with one foot on the stationary belt and walk with the other foot on the moving belt. To prevent unilateral stepping, subjects were asked to maintain a reciprocal gait pattern where

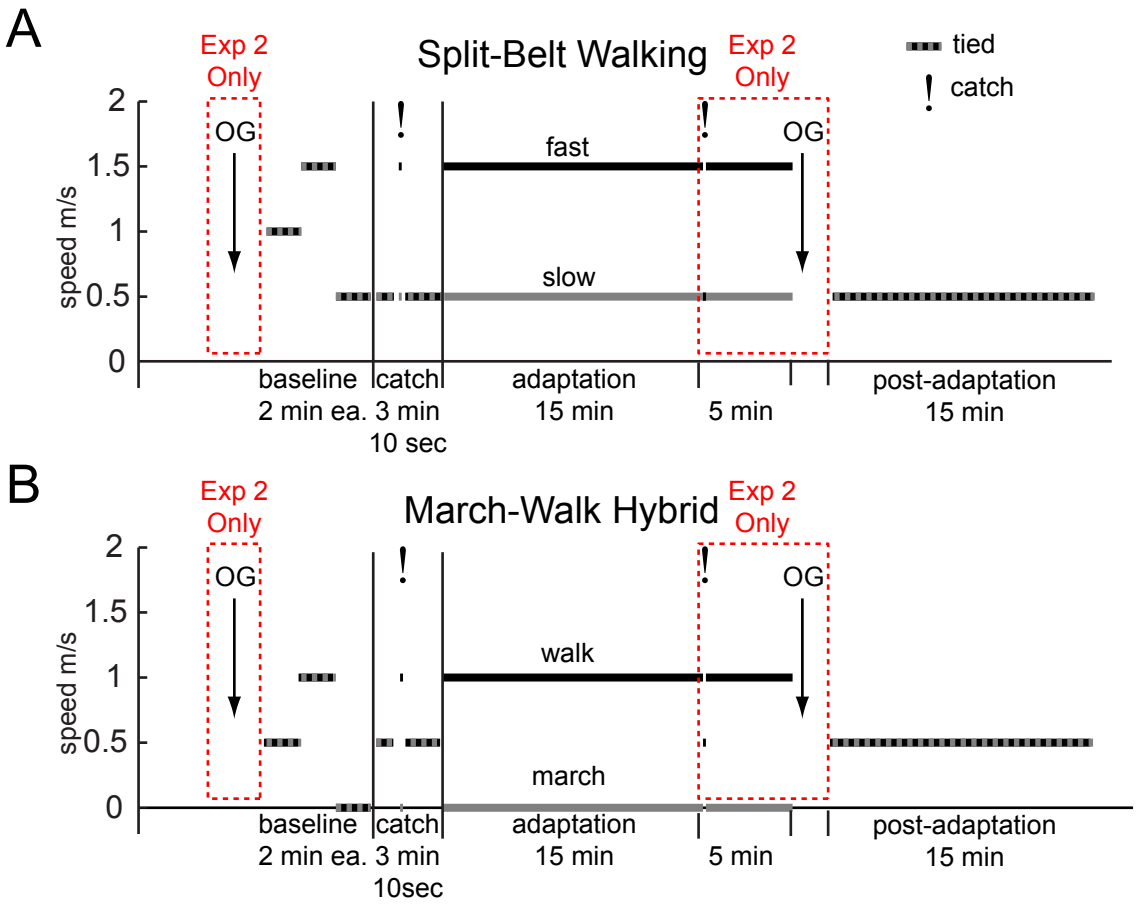

Figure 2.2: Experimental paradigms with belt speeds for (**A**) split-belt walking and (**B**) the marching-walking hybrid. Experiments began with baseline walking at three different speeds for 2 minutes each. The subjects then walked at 0.5 m/s for 1 minute, experienced a brief 10 second exposure (catch) to the belts moving at different speeds and then walked again at 0.5 m/s for 2 minutes. This was followed by an adaptation phase with the belts moving at different speeds for an extended period. In Experiment 1, subjects adapted for 15 minutes and then de-adapted on the treadmill for 15 minutes. In Experiment 2, subjects adapted for 15 minutes, experienced a 10 second tied-belt catch trial, adapted for 5 more minutes, walked over ground for ten 6 meter walks, and then returned to the treadmill for washout. For all belt speeds at 0 m/s, the subjects were instructed to march. 10 second catch trials are indicated with an exclamation mark.

stance on one leg occurred during swing on the other and vice versa. However, they were not instructed how fast to alternate feet nor how high to lift their marching foot. No explicit instructions were given to the SPLIT_TM group during split-belt walking.

Both groups in this experiment began with a 2-minute warm-up at 1.0 m/s followed by three 2-minute baselines at tied speeds (mean, fast and slow speeds). The subjects again walked at 0.5 m/s for 1 minute before they experienced an initial exposure to the belts moving at different speeds for 10 seconds. The purpose of the initial exposure was to eliminate startle effects associated with experiencing the split-belt walking for the first time (Finley et al., 2014). Although the subjects were not told that the belts would be moving at different speeds, the subjects were instructed to hold the handrail during this portion of the experiment. This brief exposure was followed by 2 minutes of walking on tied belts at 0.5 m/s. All subjects then underwent the adaptation portion of the experiment for 15 minutes with the belts moving at different speeds, followed by a post-adaptation portion for 15 minutes with tied belts. The post-adaptation speed was 0.5 m/s for both groups because previous work has shown that the largest aftereffects for split-belt training are seen at the slow speed (Vasudevan and Bastian, 2010).

In *Experiment 2*, 28 new subjects (15 male, 24.4 $\pm$ 0.9 years old) were recruited and randomly divided into two groups to assess the differences in transfer to over ground walking from the marching-walking hybrid versus standard split-belt walking. The SPLIT_OG group (n = 14) and MARCH_OG group (n = 14) adapted to the same

speeds as in Experiment 1 in a similar paradigm as shown in Figure 2.2 (note that this experiment includes the red dashed segments). Before the treadmill portion began, the subjects walked ten times over ground on a 6 meter Zeno Walkway, which recorded the time and position of over ground foot falls. After 15 minutes of adaptation on the treadmill, they experienced a 10 second tied-belt catch trial (without holding on), in which both belts moved at 0.5 m/s to assess their learning on the treadmill. Following the catch trial, they readapted for 5 more minutes. Within a few minutes of completing the adaptation portion, subjects were then pushed in a wheelchair to the Zeno Walkway, where they walked ten times over the 6 meter walkway. To measure how much over ground walking washed out treadmill adaptation, subjects were then returned with the wheelchair to the treadmill and walked for 15 minutes at 0.5 m/s. If there exists overlapping adaptive neural circuits between the marching-walking hybrid and natural walking, we should see over ground transfer following adaptation and we should see that the post-adaptation over ground walking washes out the adaptive learning (Choi and Bastian, 2007; Reisman et al., 2009).

Data analysis

In this study, step length is defined as the difference in ankle marker positions at heel strike of each leg. The heel strikes were determined from vertical ground reaction forces as crossing of a threshold corresponding to approximately 10% of each subject's weight. The fast step length corresponds to heel strike with the foot on the

fast belt and slow step length corresponds to heel strike with the foot on the slow belt as shown in Figure 2.1A. The difference in step lengths (fast - slow) is defined as step length difference. For the marching-walking hybrid, the fast leg is the walking leg and the slow leg is the marching leg as shown with step lengths in Figure 2.1B. A step length difference value of 0 means that the step lengths are equal, a positive value means that the fast step length is longer than the slow step length and a negative value means that the fast step length is shorter than the slow step length.

Time frames of interest for treadmill walking

In Experiment 1, we analyzed adaptation and post-adaptation periods in three separate time frames: initial (mean of first 5 strides), early (mean of strides 5-200) and late (mean of last 30 strides). The early measure provides a method for comparing rates of adaptation and de-adaptation between groups. This method is agnostic in that it does not assume a specific model (e.g. single or double exponential), but still allows us to robustly distinguish between groups with different rates of learning (Jayaram et al., 2012; Malone et al., 2011). Note that the baseline step length difference for each subject was calculated as the mean step length difference across the 2 minute 0.5 m/s tied-belt baseline since all groups de-adapted at this speed. The mean of this baseline period was subtracted from all subsequent analysis so that all values are expressed relative to baseline.

Over ground transfer and washout indexes

In Experiment 2, step length difference treadmill learning was defined as the difference between the mean of the first 5 strides in the tied-belt catch trial (TM_catch) and the mean of 2 minute 0.5 m/s tied-belt baseline (TM_baseline, approximately 50 strides). Baseline over ground walking (OG_baseline) was defined as the average step length difference over all ten 6 meter walks before walking on the treadmill. The post-adaptation over ground aftereffect (OG_after) was defined as the average step length difference of the first post-adaptation over ground 6 meter walk (about 4 strides). The over ground transfer was then defined as the difference between the over ground aftereffect and over ground baseline. The subjects were then returned to the treadmill to assess how over ground walking washed out the treadmill learning. The treadmill washout was defined as the difference in step length difference between TM_catch and the mean of the first 5 strides of post-adaptation on the treadmill (TM_after). These quantities were defined mathematically as

$$Treadmill\ Learning = TM_{catch} - TM_{baseline}, \tag{2.1}$$

$$Overground\ Transfer = OG_{after} - OG_{baseline}, \tag{2.2}$$

$$Treadmill\ Washout = TM_{catch} - TM_{after}. \tag{2.3}$$

Similarly, over ground transfer and treadmill washout as percentages of treadmill

learning were defined as

$$\%Overground\ Transfer = \frac{Overground\ Transfer}{Treadmill\ Learning} x100 \quad (2.4)$$

$$\%Treadmill\ Washout = \frac{Treadmill\ Washout}{Treadmill\ Learning} x100. \quad (2.5)$$

These metrics for over ground transfer are similar to those in previous split-belt experiments (Torres-Oviedo and Bastian, 2010, 2012).

Spatial and temporal contributions to adaptation

It has been shown previously that split-belt treadmill walking induces independent adaptation in the spatial domain and in the temporal domain (Malone et al., 2012). In order to further understand the differences between split-belt walking and the marching-walking hybrid, we decomposed step length difference into spatial, temporal and perturbation contributions using the following equations (Finley et al., 2015):

$$Step\ Length\ Difference = Fast\ Step\ Length - Slow\ Step\ Length \quad (2.6)$$

$$= Spatial + Temporal + Perturbation \quad (2.7)$$

where

$$Spatial = (\alpha_f - \alpha_s), \tag{2.8}$$

$$Temporal = \frac{v_s + v_f}{2}(t_s - t_f), \quad \text{and} \tag{2.9}$$

$$Perturbation = \frac{t_s + t_f}{2}(v_s - v_f). \tag{2.10}$$

Here, α_s is a spatial variable that indicates where the slow foot is placed relative to the previous fast foot placement, v_s is the approximate speed of the slow ankle relative to the body while it is on the slow moving belt, and t_s is the slow step time. Similarly, α_f is a spatial variable that indicates where the fast foot is placed relative to the previous slow foot placement, v_f is the approximate speed of the fast ankle relative to the body while it is on the fast moving belt, and t_f is the fast step time. The step time was defined as the time between opposite heel strikes as done previously by Malone et al (Malone et al., 2012). The derivation of this model has been described in detail elsewhere (Finley et al., 2015) and is summarized in the Appendix A for clarity.

In this model for step length difference, the spatial contribution is due to differences in foot placements relative to the body, the temporal contribution is due to differences in step times, and the perturbation contribution is largely due to differences in treadmill belt speeds. Under normal treadmill walking, individuals do not experience the perturbation term because both feet are moving at the same speed

($v_s = v_f$). During split-belt walking, this term can be thought of as a perturbation to step length difference as it changes almost instantly to a non-zero value when the belts begin moving at different speeds. The temporal and spatial components must cancel this perturbation to have symmetric step lengths; therefore, we also calculated the sum of the temporal and spatial components. Baseline values from the 0.5 m/s tied baseline for each of these components were subtracted to account for any offset. Since each subject has a slightly different perturbation size, we also calculated the relative contribution of the temporal and spatial components with respect to the perturbation size.

Statistical analysis

In Experiment 1, a mixed model repeated measures ANOVA with time frames (initial adaptation, early adaptation, late adaptation, initial post-adaptation, early post-adaptation and late post-adaptation) and group (split-belt walking or marching-walking hybrid) as fixed effects and subject as a random effect was utilized to test for differences in step length during the experiment. When there was statistical significance in this ANOVA, post-hoc analyses were used to compare between time frames (1 sample t-tests) and between groups (2 sample t-tests). One subject from SPLIT_TM group was removed from all analyses since the subject experienced an initial adaptation step length difference that exceeded 3 standard deviations of the other SPLIT_TM subjects. For the model analysis, 1 sample t-tests were used to

compare between time frames within a group and 2 sample t-tests were used to compare between the groups for each of the model components for several time frames. In Experiment 2, 2 sample t-tests were used to analyze the overground metrics discussed above. All statistical analysis was conducted in Matlab and p values less than 0.05 were considered as significant.

2.2 Results

Time frame analysis

We found that the marching-walking hybrid induces adaptation and aftereffects of step length difference, similar to those seen with split-belt walking. Figure 2.3A shows the group means (± standard error) on a stride by stride basis for step length difference for Experiment 1. Both groups had similar step length differences during baseline tied-belt walking at 0.5 m/s ($p = 0.41$) which were not different than 0 ($p = 0.14$), i.e. symmetric walking. Therefore, baseline step length difference was removed on an individual basis. The initial, early, and late time frames for adaptation and post-adaptation are shown in Figure 2.3B. A mixed model repeated measures ANOVA showed that there was not a significant group effect ($F(1, 26) = 0.77, p = 0.38$), but there was a significant time frame effect ($F(5, 130) = 408, p < 0.001$) and a group by time frame interaction effect ($F(5, 130) = 8.8, p < 0.001$). These effects indicate that the step length differences varied across time frames and that these

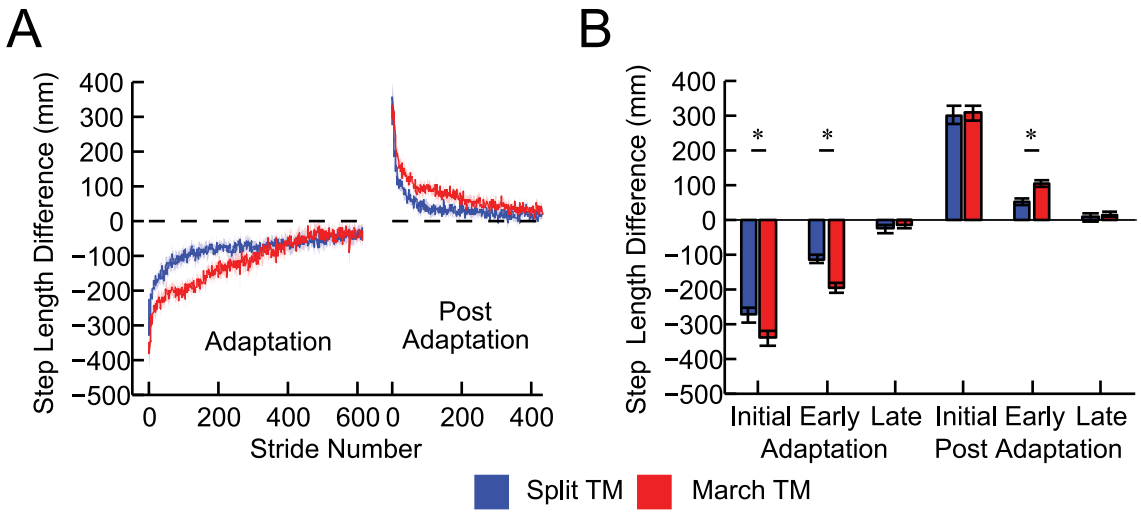

Figure 2.3: Experiment 1 Results. (**A**) The mean (± standard error) stride-to-stride step length difference for the SPLIT_TM and MARCH_TM groups. The step length difference is baseline subtracted on an individual basis. During adaptation, the step length difference is initially perturbed and then slowly adapted to near baseline values. During post-adaptation the belts are returned to the same speed and an after-effect is observed in the opposite direction. The MARCH_TM and SPLIT_TM group are shown in red and blue, respectively. (**B**) Analysis for initial adaptation, early adaptation, late adaptation, initial post-adaptation, early post-adaptation and late post-adaptation. Significant differences ($p < 0.05$) are represented with an asterisk.

changes across time frames depended on the group. Post hoc t-tests showed that the MARCH_TM group had a larger step length difference during initial adaptation ($p = 0.04$), early adaptation ($p < 0.001$) and early post-adaptation ($p = 0.002$) compared to the SPLIT_TM group, whereas no differences were observed for late adaptation ($p = 0.52$), initial post-adaptation ($p = 0.88$) and late post-adaptation ($p = 0.46$). A striking finding is that it took the marching-walking hybrid group longer to reduce the step symmetry errors in both adaptation and post-adaptation as shown by the differences in the early time frames.

Step length difference model analysis

We applied the step length difference model described in the Methods to determine if there were differences in the temporal, spatial and perturbation components across time frames or between groups. Stride-by-stride adaptation and post-adaptation group mean ($\pm$ standard error) for the spatial, temporal and perturbation components as well as step length difference for the SPLIT_TM and MARCH_TM groups are shown in Figure 2.4A and Figure 2.4B, respectively. These figures demonstrate that the temporal component adapts much quicker for both groups whereas the spatial component changes much slower. Also note that the SPLIT_TM group has approximate equal contributions from the spatial and temporal components at the end of adaptation, whereas the MARCH_TM group has a much greater contribution from the spatial component.

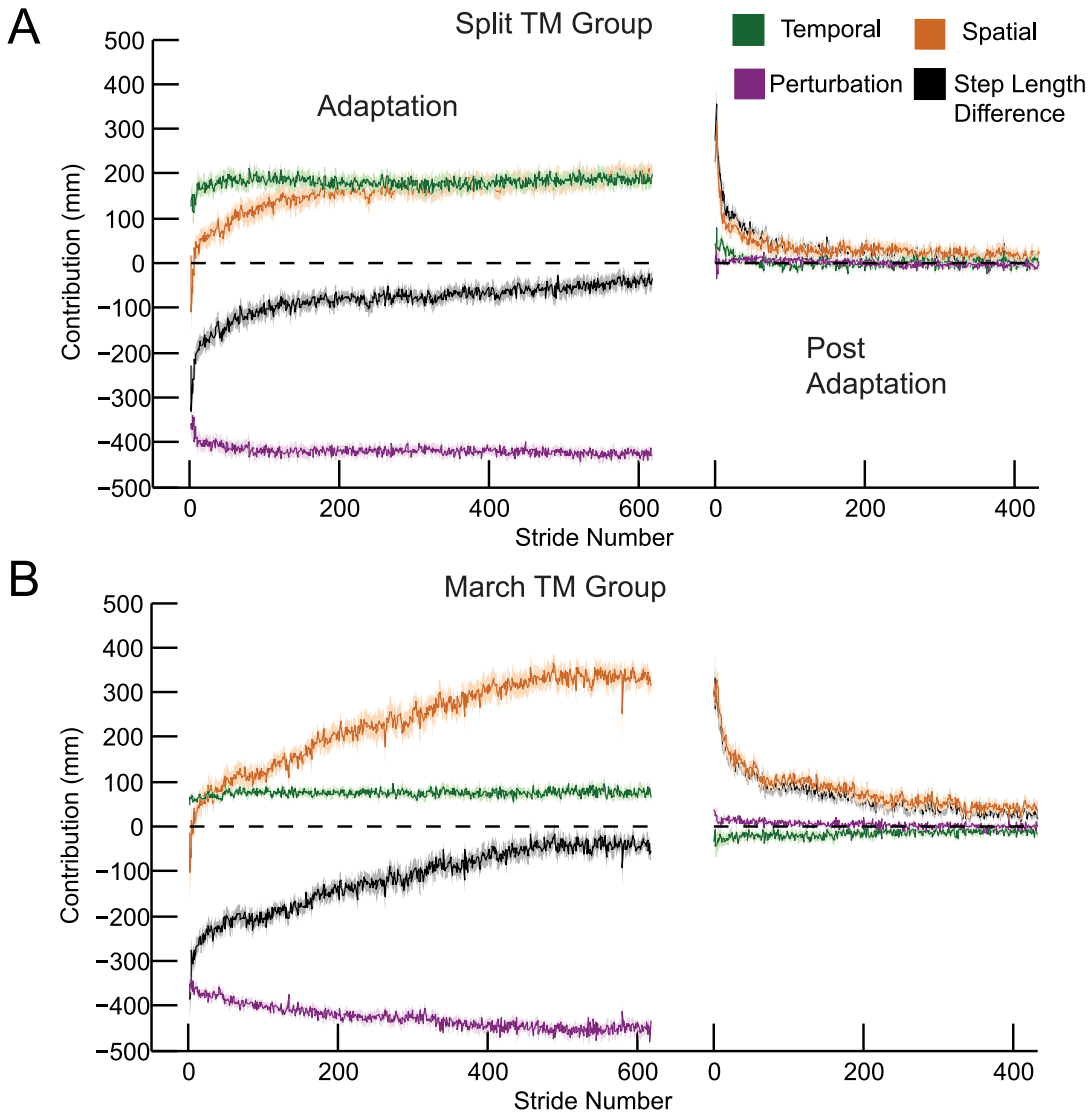

Figure 2.4: Model Results Experiment 1. The step length difference, fast slow, (black) can be decomposed into a spatial (orange), temporal (green) and perturbation (purple) contribution. (**A**) The split-belt walking group averages ± standard error. (**B**) The marching-walking hybrid group averages ± standard error. The perturbation (largely negative) occurs when the treadmill belts are driven at different speeds. The temporal term adapts faster in both groups and is much greater in the split group. The spatial term adapts slower and is greater in the marching-walking hybrid group.

With this model, we can explain the differences in Experiment 1 observed in initial adaptation in step length difference. There was no significant difference between the groups during initial adaptation in the spatial component ($p = 0.97$), the sum of the spatial and temporal components ($p = 0.11$) nor the perturbation ($p = 0.84$), but there was a significant difference in the temporal component ($p = 0.005$) as shown in Figure 2.5A. This indicates that the initial difference observed in step length difference ($p = 0.04$) is due to the temporal component. Recall that the temporal component is the product of the average belt speed and the step time difference. Although there was no difference in the step time difference ($p = 0.80$) during initial adaptation, the average speed was significantly different ($p < 0.001$) near 0.5 m/s for the marching-walking hybrid and near 1.0 m/s for the split-belt walking. As a result, it appears that the difference between these two groups in initial adaptation step length difference (Figure 2.3) was due to the difference in average belt speed since all other components of this model were not significantly different.

We observed that different spatial and temporal strategies can achieve symmetric stepping in late adaptation for the two groups. Figure 2.5B shows the different model components of step length difference for late adaptation. Over the course of 15 minutes, both groups increased their spatial component (late $-$ initial adaptation both $p < 0.001$) but to different extents as the MARCH_TM group has a much larger value compared to the SPLIT_TM group ($p < 0.001$). In addition, the MARCH_TM group does not significantly change its temporal component (late $-$ initial adapta-

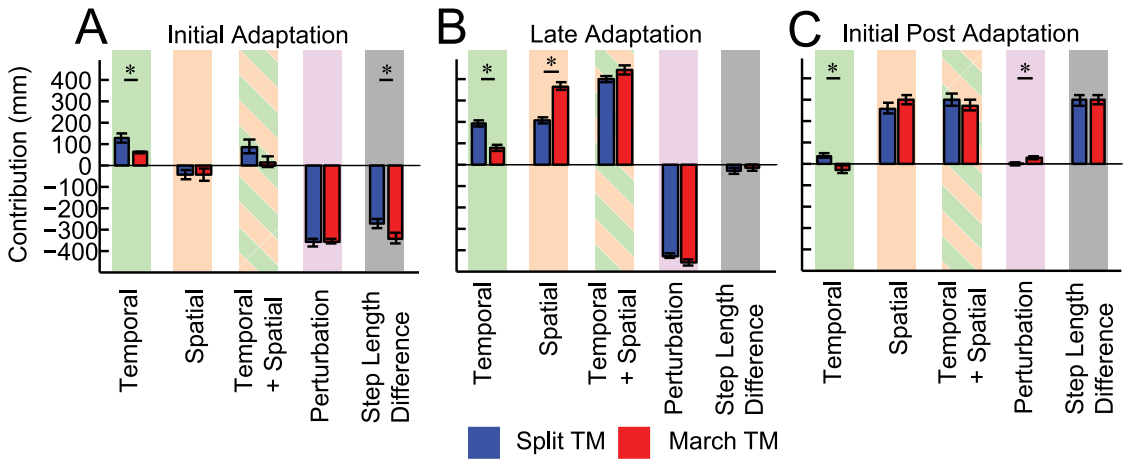

Figure 2.5: Model Results Experiment 1. The step length difference, fast − slow, (black) can be decomposed into a spatial (orange), temporal (green) and perturbation (purple) contribution. The temporal, spatial, sum (temporal plus spatial), perturbation and step difference components were analyzed for (**A**) initial adaptation, (**B**) late adaptation, and (**C**) initial post-adaptation of Experiment 1.

tion, $p = 0.15$), whereas the SPLIT_TM group significantly increases its temporal component (late − initial adaptation, $p < 0.001$). However, these spatial and temporal changes balance out since the sum of the two components in late adaptation are not significantly different ($p = 0.13$). Although the perturbation is not significantly different between the two groups at late adaptation ($p = 0.07$), the perturbation has increased slightly (both $p < 0.001$), most likely due to a settling of the stride times. During late adaptation, the sum of the temporal and spatial components is almost equal and opposite to the amplitude of the perturbation, so the groups ultimately reach a similar step length difference ($p = 0.52$). Figure 2.6 shows the relative contributions of the temporal and spatial components to offsetting the perturbation during late adaptation. These results indicate that individual subjects can use different combinations of the spatial and temporal components to achieve symmetric stepping. It appears that subjects performing the marching-walking hybrid utilize a strategy that is mostly spatial whereas the subjects walking with the split belts use a more even mixture of temporal and spatial. However, subjects in either group could vary in their strategy.

Which components are stored when the belts return to tied speeds? The right portion of Figure 2.4A and Figure 2.4B show the components for post-adaptation in Experiment 1. Figure 2.5C shows that initial aftereffects in step length difference are largely due to the spatial component. The spatial component remains largely positive and is not significantly different between the two groups ($p = 0.27$). After adaptation,

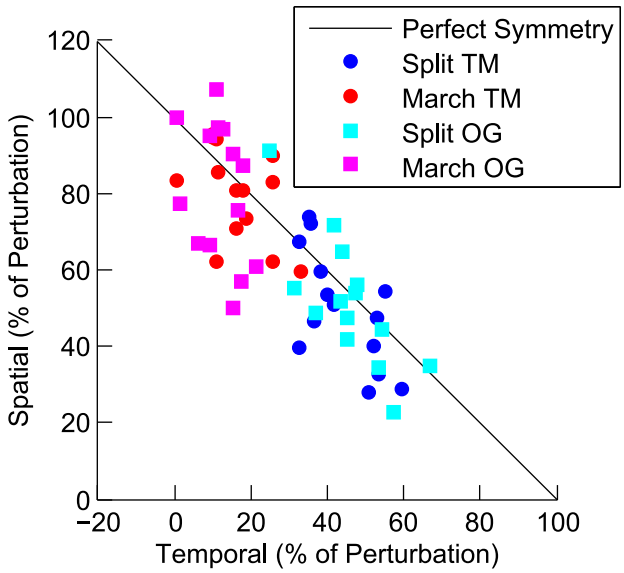

Figure 2.6: Model Relative Contribution in Late Adaptation (last 30 strides after 15 minutes of adaptation). The temporal and spatial components each cancel some percentage of the perturbation. Perfect symmetry is represented with a black line, meaning that anywhere along the line a subject is walking symmetrically. These data indicate that the marching-walking hybrid subjects utilize a strategy that is mostly spatial whereas the split-belt training subjects use a strategy that is a mixture of both temporal and spatial. Relative contributions are shown for groups from both Experiment 1 and Experiment 2.

the belts are returned to the same speed so the perturbation term is near zero for both groups. There is a significant difference between the two groups in perturbation ($p = 0.01$) and in the temporal component ($p = 0.004$), but since these terms are relatively small their effects on the overall step length difference are minimal. Thus, there is no significant difference between the two groups in the sum of the spatial and temporal terms ($p = 0.52$) nor in the overall step length difference ($p = 0.88$). As a result, the positive aftereffect in step length difference was due almost exclusively to the spatial component as can be seen inFigure 2.4A and Figure 2.4B.

Over ground walking analysis

In Experiment 2, we assessed both adaptation and over ground transfer for a new group of subjects. Figure 2.7A shows baseline subtracted step length difference results for the treadmill segments. Both groups again have similar baseline tied-belt walking ($p = 0.18$) which was not different than 0 ($p = 0.32$). With these new groups of subjects, we confirmed the results of Experiment 1 that the marching-walking hybrid had a larger initial adaptation step length difference ($p = 0.03$), adapted slower ($p < 0.001$) and de-adapted slower ($p = 0.07$). We also observed again that the marching-walking hybrid utilized a strategy that was mostly spatial as shown with the relative contributions of the temporal and spatial components compared to the perturbation in Figure 2.6.

The main objective of Experiment 2 was to compare the over ground transfer

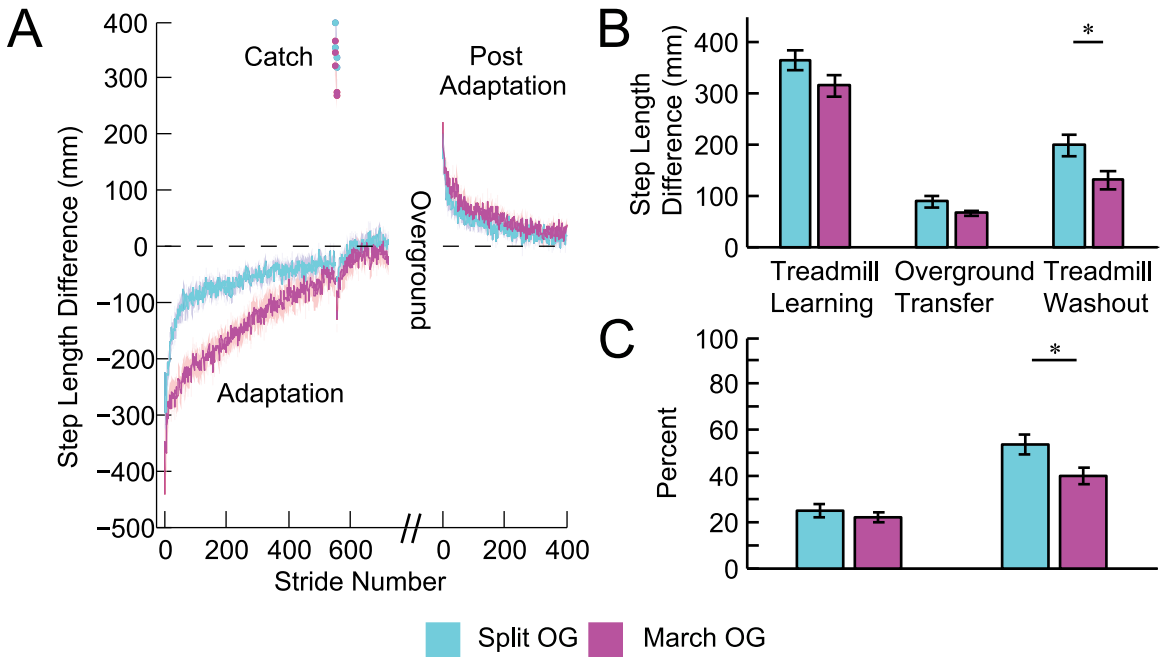

Figure 2.7: Experiment 2 Results. (**A**) The mean stride-by-stride step length difference for the treadmill portion of the split and march groups. (**B**) The step length difference for treadmill learning, over ground transfer and treadmill washout for the two groups. (**C**) Over ground transfer and treadmill washout relative to the treadmill learning. The marching-walking hybrid group is shown in magenta and the split group is shown in cyan.

and treadmill washout between the two groups. We did not observe a difference in the amounts of treadmill learning between the groups ($p = 0.11$). There was significant over ground transfer in both groups relative to baseline (both $p < 0.001$). Furthermore, the amount and percentage of transfer to over ground walking was not significantly different between the groups ($p = 0.09$, $p = 0.45$, respectively) as shown in Figure 2.7B and Figure 2.7C, respectively. On the other hand, the amount of treadmill washout was reduced in the marching-walking hybrid for both absolute ($p = 0.03$, see Figure 2.7B) and percent ($p = 0.03$, see Figure 2.7C). In summary, the marching-walking hybrid group in Experiment 2 transferred similarly to over ground walking compared with the split-belt walking group, but washed out treadmill after-effects less.

2.3 Discussion

The objective of this study was to compare a marching-walking hybrid (in which one foot marches on a stationary surface and the other foot walks on a moving treadmill belt) to standard split-belt walking. In Experiment 1, we demonstrated that the marching-walking hybrid does induce adaptation and produces aftereffects in step length differences comparably to that of split-belt walking. In addition, we observed in this experiment that subjects in the marching-walking hybrid adapted slower and de-adapted slower. In Experiment 2, we observed that the marching-walking hybrid

does transfer to over ground walking to a similar extent as split-belt walking, but washes out less. We also observed that the marching-walking hybrid groups utilize a spatial strategy whereas the split-belt walking groups utilize a spatiotemporal strategy to counter the perturbation induced by the belts moving at different speeds.

The marching-walking hybrid presented here is similar to a reduced gait used in previous locomotor studies. In a reduced gait, one limb is walking on a moving treadmill belt while the other limb is held "stiff" and steps in place (Faist et al., 1999; Van de Crommert et al., 1996). The marching-walking hybrid is slightly different in that the marching leg is not required to be stiff and allows flexion of the joints during the marching swing phase. In the work by Faist and colleagues, they demonstrated that the biceps femoris reflex as well as EMG signals of the lower limbs exhibited phase-dependent modulation (Faist et al., 1999; Van de Crommert et al., 1996). These signals were shown to be quite similar in the "stiff" leg to that of normal gait even though the stiff leg had little to no joint movement. Given the work in a reduced gait as well as the similarities in adaptation between the groups presented here, this suggests that there may be partial overlap in the neural circuits governing adaptation in the marching-walking hybrid and split-belt walking.

Sensory signals important for locomotion

While these neural circuits may be similar between the groups studied here, the peripheral sensory signals experienced during the marching-walking hybrid are likely

different from those of split-belt walking. Previous work in cats has demonstrated that extension of the hip as well as unloading of the stance leg are both important neural signals that influence the stance-to-swing transition (Andersson and Grillner, 1981, 1983; Duysens et al., 2000; Duysens and Pearson, 1976, 1980; Grillner and Rossignol, 1978; McVea et al., 2005). This work has indicated that the stance leg needs to be extended and unloaded before flexion will begin. Additionally, these signals influence this transition even without input from the cerebral cortex, suggesting that some temporal elements of locomotion are controlled by subcortical circuits (possibly in the spinal cord) (Andersson and Grillner, 1981, 1983; Grillner and Rossignol, 1978). Similarly, it was shown in human infants that there is an inverse relationship between loading and limb extension that initiated this transition from stance to swing (Pang and Yang, 2000). In our marching-walking hybrid, this unloading signal is still present in the transfer of weight to the moving limb, but there is little to no hip extension. This suggests that bilateral hip extension is not required to produce post-adaptation effects in step length difference for healthy adults.

While most prior locomotion work has focused on sensory signals at the stance to swing transition, locomotor learning requires feed-forward adjustments and this type of learning has been recently shown to be related to variables associated with heel strike (Malone et al., 2012). However, little work has investigated the important neural signals at heel strike required for adaptation. While the neural signals are not recorded in this study, we can still make inferences based on the spatial-temporal

balance of step length difference.

Spatial-temporal balance of step length difference

Previous work from our lab has shown that split-belt walking adaptation contains a form of error-based learning and depends on the cerebellum (Morton and Bastian, 2006). We have suggested that step length asymmetry, or the difference in step lengths, serves as an error signal driving learning (Reisman et al., 2005). Additionally, it has been shown that people adapt both spatially ("where to step") and temporally ("when to step")(Malone et al., 2012). Here we used a step length difference model that separates the treadmill perturbation (i.e. difference in treadmill belt speeds) from the spatial and temporal components involved in re-establishing step symmetry during adaptation. Importantly, both of the groups studied here received similar levels of perturbation to step length difference, yet adjusted their spatial and temporal components differently in order to adapt. Here we refer to the perturbation as the size of the perturbation component and not the size of the initial step length difference. To cancel this perturbation, subjects in the marching-walking hybrid group used a strategy that was largely spatial whereas the split-belt group used a strategy that was a mixture of both spatial and temporal components. Previous work has also shown that split-belt walking uses a spatial-temporal strategy (Finley et al., 2015). By comparing the marching-walking hybrid and split-belt walking paradigms presented here, this demonstrates that people are able to counter a perturbation of a particular

size by varying their temporal and spatial strategies.

Fast adapting temporal component

While the size of the temporal component in late adaptation was different between the marching-walking hybrid and split-belt walking, the temporal component adapted quickly in both conditions. A fast adapting temporal component is consistent with previous split-belt work in cats (Forssberg et al., 1980; Frigon et al., 2013), infants (Pang and Yang, 2000) and adults (Dietz et al., 1994; Malone et al., 2012; Reisman et al., 2005). In both infants and decerebrate cats, there is a reduction or absence of strong descending input from the cerebral cortex. This suggests that the spinal cord may be selecting these temporal phase switches simply based on the belt speed for each foot. This is further supported by recent work in decerebrate cats which demonstrates linear relationships between split-belt speeds and the times of stance and swing (Frigon et al., 2013). Given that each belt speed is different between the marching-walking hybrid and split-belt walking, it is possible that the observed differences in the size of the temporal component of our step length difference model may simply be a result of some relationship in the belt speed combinations and this relationship may be calculated in the spinal cord.

Slow adapting spatial component

In the work presented here, we observed that the spatial contribution to adaptation was larger in the marching-walking hybrid than in split-belt walking. Since the temporal component is established first, it is possible that the desired spatial component is then properly adjusted to result in symmetric walking. We predict that the cerebellum is involved in updating this spatial component based on evidence that (1) people with cerebellar damage do not show learning or aftereffects in step length symmetry (Morton and Bastian, 2006) and (2) the aftereffect observed here is largely based on the spatial component. This is also supported with work by Jayaram and colleagues, who demonstrated that brain stimulation with transcranial direct current stimulation applied over the cerebellum could modulate the rates of spatial learning but not temporal learning (Jayaram et al., 2012).

Rates of step length adaptation and de-adaptation

In this work, we observed in both experiments that the marching-walking hybrid had larger (more negative) early step length differences. In post-adaptation, we observed a significant early step length difference in Experiment 1 and a near significant early step length difference in Experiment 2. These results suggest that subjects performing the marching-walking hybrid adapted slower and de-adapted slower. It is possible that the rates of adaptation and de-adaptation are a direct result of the

locomotion behavior, but it is also possible that the belt speed ratio (infinite for the marching-walking hybrid vs. 3:1 for split-belt walking) may play a role even though we fixed the difference in belt speeds at 1.0 m/s for both groups. This is supported by previous work which showed that greater belt speed ratios resulted in slower adaptation rates (Reisman et al., 2005). Future work with different fast belt speeds for the marching-walking hybrid could be conducted to investigate this further.

Previous studies have indicated that the rate of adaptation can be heavily influenced by the degree to which the executive system is involved in the adaptive behavior (Taylor and Thoroughman, 2008). Recently, it was shown in a split-belt experiment that conscious correction of step lengths increased adaptation rates whereas distraction in a dual-task slowed adaptation rates (Malone and Bastian, 2010). This work also demonstrated that distraction during adaptation resulted in a slower de-adaptation rate. With this in mind, it is possible that requiring subjects to march on the stationary belt may distract from the locomotor adaptation process, increasing the early step length differences in adaptation and post-adaptation of the marching-walking hybrid groups.

Comparison with unilateral stepping

Recently, it was shown that unilateral stepping, in which one foot remains on a stationary surface and the other foot walks on a moving belt, has modest transfer to over ground walking for stroke survivors (Kahn and Hornby, 2009) and is reduced in

healthy controls as compared to split-belt walking (Huynh et al., 2014). Based on the work in reduced gait (Faist et al., 1999; Van de Crommert et al., 1996), it is possible that the muscle activation patterns are similar across unilateral stepping, marching-walking hybrid, and split-belt walking; however, the unilateral stepping does not have alternating single support periods which is known to be an important sensory signal. Thus, it is possible that the presence of this unloading signal in the marching-walking hybrid may result in a slight increase in overground transfer as observed here in Experiment 2. This is supported by previous work that shows that transfer can be improved if context cues that signal the differences between adaptation and the natural environment are reduced (Kluzik et al., 2008; Torres-Oviedo and Bastian, 2010, 2012). While a direct comparison between our between-subject design and the unilateral stepping within-subject design by Huynh and colleagues cannot be conducted, it is important to know that both unilateral stepping and the marching-walking hybrid both produce post-learning effects and potentially could be used for rehabilitation as an alternative to split-belt walking as done by Kahn and colleagues (Kahn and Hornby, 2009).

Clinical implications

Cerebral stroke survivors are known to walk with an asymmetric gait (Allen et al., 2011; Balasubramanian et al., 2007; Hall et al., 2012; Patterson et al., 2010). In our recent work, we observed that stroke survivors can have baseline asymmetries in

the spatial, temporal and perturbation contributions of our step length difference model (Finley et al., 2015). Additionally, some stroke survivors have gone through rehabilitation to walk symmetrically, but their new strategy typically is to compensate for the existing asymmetry in one term by modifying another term. For example, if they have a negative temporal term asymmetry, they might increase their spatial term to compensate instead of bringing the temporal term back to zero. This means that the individual will be walking with equal step lengths, but using a different strategy than healthy controls. The work here supports the idea that different strategies can be utilized to walk with symmetric step lengths.

Previous work has shown that split-belt treadmill walking can improve step length asymmetry in stroke survivors (Reisman et al., 2013, 2007, 2009). However, split-belt treadmills are generally expensive and not easily accessible. In this study, we demonstrated that short-term training with a marching-walking hybrid induces similar adaptation and aftereffects to that of split-belt walking in healthy individuals. This suggests that a marching-walking hybrid rehabilitation strategy could possibly be used when split-belt treadmills are not available. In addition, since the marching-walking hybrid focuses on spatial adaptation, it is possible that patients with spatial asymmetries may benefit more from this type of training. Future work will be conducted to determine if we see similar experiences in stroke survivors.

Acknowledgements

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Chapter 3

Blocking trial-by-trial error correction does not interfere with motor learning in human walking

The human nervous system uses a repertoire of learning mechanisms to change walking patterns to account for a variety of environments and situations. For example, we explicitly think about where to place our feet when stepping on stones in a river, but adapt more implicitly to walking in snow. We currently do not understand how these explicit and implicit processes interact when they are put in conflict or engaged towards the same learning goal. For example, if an explicit strategy is used to block the expression of implicit learning, does the latter still occur? Here, we studied the interactions between these explicit and implicit processes using a strategy via visual

feedback and a split-belt treadmill, respectively.

When subjects walk on a split-belt treadmill with one belt moving faster than the other, they learn a new gait pattern over hundreds of steps by changing where and when they place their feet on the treadmill (Finley et al., 2015; Long et al., 2015; Reisman et al., 2005). When the treadmill belts are then returned to the same speed, post-learning effects are observed such that subjects retain much of the newly learned spatial pattern that then decays over a couple hundred steps (Reisman et al., 2005). This learning is largely implicit, particularly when the perturbation is gradually introduced (Sawers et al., 2013; Torres-Oviedo and Bastian, 2012) — subjects are often unaware that there is a perturbation for much of the learning period. Additionally, subjects are hard pressed to describe how their walking is changing during this process and they are surprised that they have post-learning effects once the perturbation is abruptly removed.

It is generally believed that these post-learning effects result from the updating of an implicit, cerebellar-driven internal model of how the body should move in an environment (Morton and Bastian, 2006; Wolpert et al., 1995). Recently, we showed that online visual feedback of the walking pattern accelerates adaptation to an abrupt perturbation during split-belt treadmill walking (Malone and Bastian, 2010), suggesting that explicit and implicit learning processes can work together to more quickly recalibrate gait to a new environment. However, since the rate of learning was not controlled in that study, it is still unknown how an explicit strategy influences the

post-learning effects.

In this study, we asked if explicit strategies monitored via visual feedback with a controlled learning rate would influence the post-learning effects typically observed as a result of implicit learning. We compared the effects of providing explicit strategies that were either incongruent or congruent with the goal of implicit learning (i.e., reducing step length asymmetry). It is important to note that computational models of this type of implicit motor learning all require that the behavior change from one trial to the next (Mazzoni and Krakauer, 2006; Taylor and Ivry, 2011; Taylor et al., 2010). As such, we hypothesized that explicitly blocking the expression of a new gait pattern using incongruent visual feedback should prohibit implicit learning such that no post-learning effects are observed once the belts return to the same speed. Data supporting this hypothesis has been shown previously for blocking learning in an abrupt split-belt paradigm (Malone et al., 2012). Surprisingly, we observed that blocking expression of the new pattern during gradual learning was not sufficient to block the post-learning effects, but rather the post-learning effects were completely unaffected by the clamping of the motor output during learning. Furthermore, we also observed that congruent visual feedback (i.e. a coach) neither enhances nor interferes with the post-learning effects. These striking results suggest that we can implicitly learn a new walking pattern without ever changing our motor output during the learning phase.

3.1 Methods

Subjects

50 healthy adults (32 female, 18 - 38 years old) gave informed written consent before volunteering for this study. The Johns Hopkins Institutional Review Board approved all protocols.

Overall protocol

All subjects walked on a split-belt treadmill, some with additional visual feedback provided on a television screen (1.25 m by 0.69 m) placed in front of the treadmill as shown in Figure 3.1A. The visual feedback and treadmill belt speeds were controlled with custom software (Vizard, WorldViz). We refer to the portions of the experiment in which the belts moved at the same speed as "tied-belts" and different speeds as "split-belts." During split-belt walking, the right belt moved faster than the left. A thin board was placed between the two belts to prevent subjects from stepping from one belt to the other. To prevent falling, subjects wore a non-load bearing safety harness attached to the ceiling and held onto the treadmill's handrail for a few seconds at the beginning and end of each walking trial. During most portions of the experiment, subjects were instructed to avoid looking at their feet and to instead look at the display screen while they were walking. One group of subjects as described

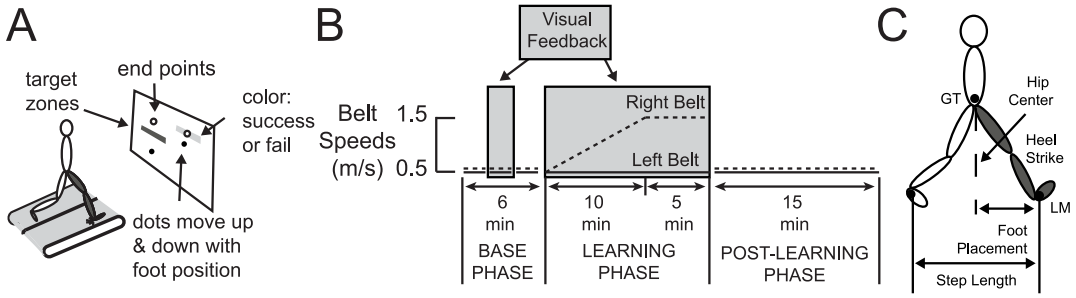

Figure 3.1: (**A**) Experimental set-up with a split-belt treadmill and a visual feedback display. The visual feedback indicated the foot position, target zones and foot placement (end points). The target zones turned green for success and red for failure. (**B**) The treadmill belt speeds as a function of time for the baseline, learning and post-learning phases. The visual feedback was displayed for the grey portions. (**C**) Foot placement is defined as the distance between the hip center and the ankle at heel strike. Step length is defined as the distance between the two ankles at heel strike. Tracking markers were placed bilaterally on the greater trochanter (GT) and lateral malleolus (LM).

below was instructed to look at their feet during learning. Occasionally, the visual feedback was not displayed and subjects were allowed to watch a movie or show on the display.

Subjects completed a basic paradigm that consisted of a baseline phase, learning phase, and post-learning phase (see Figure 3.1B). The baseline phase consisted of 2 minutes of walking without visual feedback, 2 minutes of walking with visual feedback, and 2 minutes of walking without visual feedback. The baseline period with visual feedback was used to familiarize the subjects with the visual feedback. The belt speeds were tied at 0.5 m/s during all parts of the baseline phase.

During the learning phase, the right treadmill belt was gradually increased over a period of 10 minutes from 0.5 m/s to 1.5 m/s by increasing the right speed every 3 seconds and then held constant for 5 more minutes as shown in Figure 3.1B. The left treadmill belt was held constant at 0.5 m/s during this period. All subjects received a short break every 5 minutes. The subjects received visual feedback during the learning phase (unless specified below). We decided to use a gradual learning paradigm because it 1) allows us to control the rate of learning and 2) previous split-belt work has demonstrated that conscious correction with feedback modulates the rate of learning and may interact with post-learning effects (Malone and Bastian, 2010). By controlling the rate of learning, we can confidently compare the post-learning effects from multiple feedback experiments.

For all experiments, the post-learning phase consisted of 15 minutes of tied-belt

walking at 0.5 m/s with no visual feedback and with no breaks. This post-learning speed was selected as it has shown to produce the largest post-learning effects (Vasudevan and Bastian, 2010). The treadmill was stopped briefly between the learning phase and post-learning phase for safety reasons and to turn off any feedback. Prior to beginning the post-learning phase, subjects were not told whether the belt speeds would change and they were instructed to "do whatever felt natural." This allowed us to measure the automatic post-learning effects without a specific explicit strategy.

Data collection

Three-dimensional kinematic data of infrared-emitting markers was recorded at 100 Hz (filtered with a fourth order Butterworth filter) with an Optotrak motion capture system (Northern Digital). Markers were placed bilaterally over the lateral malleolus and greater trochanter as shown in Figure 3.1C. Subjects walked on a split-belt treadmill (Woodway Split-Belt treadmill) that was equipped with a vertical force sensor under each belt. These forces were recorded at 1000 Hz (smoothed by 5 time steps) and were synchronized with the motion capture data. The forces were used to detect heel-strike events as a threshold crossing of approximately 10% of the subject's weight. The kinematic data and forces were used in real-time in calculation of the visual feedback provided to some of the subjects.

Gait parameters

It has been shown previously that split-belt adaptation induces learning to reduce step length asymmetry (Finley et al., 2015; Long et al., 2015; Malone and Bastian, 2010; Reisman et al., 2005). Here step length is defined as the anterior-posterior distance between the ankle markers at heel strike as shown in Figure 3.1C. The fast step length refers to step length at heel strike on the fast belt and slow step length refers to step length at heel strike on the slow belt. We have previously shown that the differences in step lengths can be decomposed into the sum of spatial, temporal and perturbation contributions (Finley et al., 2015; Long et al., 2015).

$$\begin{aligned} Step\ Length\ Difference &= Fast\ Step\ Length - Slow\ Step\ Length & (3.1) \\ &= Spatial + Temporal + Perturbation & (3.2) \end{aligned}$$

For a derivation of this decomposition see our previous work (Finley et al., 2015; Long et al., 2015). The spatial term is based on where subjects place their feet relative to their body at heel strike

$$Spatial = \alpha_f - \alpha_s \tag{3.3}$$

where α_f is where the fast foot is placed relative to the previous slow foot placement and α_s is where the slow foot is placed relative to the previous fast foot placement. We define foot placement as the anterior-posterior distance (mm) between the ankle at heel strike and the average of the two hip markers as shown in Figure 3.1C. The

temporal term is based on the difference in step times

$$Temporal = \frac{v_s + v_f}{2}(t_s - t_f) \tag{3.4}$$

where t_s is the slow step time, t_f is the fast step time, v_s is the average speed of the slow ankle relative to the body during the slow step time and v_f is the average speed of the fast ankle relative to the body during the fast step time. Note that the step times is in time units (s), and therefore must be multiplied by the average speeds (mm/s) in order to compute how they contribute to the step length asymmetry (mm). We define step time as the time between heel strikes on opposite sides of the body. The perturbation term is based on the difference in belt speeds.

$$Perturbation = \frac{t_s + t_f}{2}(v_s - v_f) \tag{3.5}$$

Throughout all phases of the experiment, we calculate step length difference as well as the spatial, temporal and perturbation contributions.

In our previous work, we showed that the spatial and temporal terms adapt to cancel an abrupt split-belt perturbation in order to reduce step length differences (Finley et al., 2015; Long et al., 2015). Additionally, we observed that the post-learning step length differences were dominated by changes in the spatial term – the temporal and perturbation terms were small and decayed rapidly (Long et al., 2015). This is also true as shown here for a gradual split-belt learning protocol — the

spatial term explains a majority of the post-learning effect in step length difference (see Figure 3.2). Therefore, we were interested in providing visual feedback about foot placement to add explicit strategy to the split-belt walk protocol and will focus primarily on the spatial component throughout the manuscript. Experiments with temporal feedback have been previously attempted but prior work has suggested that subjects may not be able to consciously adjust their gait timing to a resolution similar to that of spatial parameters (Malone et al., 2012).

Visual feedback

The visual feedback provided on the display showed foot position of each side of the body. The display (Figure 3.1A) provides feedback to the subject about the real-time foot position relative to the body, foot placement at heel strike (end points), and target zones (horizontal bars). The color of target zones briefly showed success (green) or failure (red) at heel strike. The width of each target zone was set at 4 cm for all subjects. The subjects were able to see where they stepped relative to the targets, so they were easily able to determine directional information from the end-point feedback. The feedback display focused on the heel strike instead of the toe-off because previous work has suggested that parameters associated with heel strike adapt in a feedforward manner, whereas parameters associated with toe-off do not exhibit typical motor output behavior (Malone et al., 2012).

Experimental groups

Subjects were randomly divided into five different groups. The first group IMPLICIT_ONLY (n = 10) performed the gradual split-belt learning protocol shown in Figure 3.1B while watching TV (i.e. no visual feedback). This group served as a no-feedback control for comparison in all experiments in this study. Since this group did not receive visual feedback, the baseline phase consisted of only 2 minutes of walking.

A second group of subjects INCONGRUENT (n = 10) was tested with the split-belt protocol shown in Figure 3.1B and with visual feedback displayed on the screen. Both the left and right target locations did not change during the learning phase and were fixed at the average foot placements for the baseline of the IMPLICIT_ONLY group. Another group LOOK_DOWN (n = 10) performed a similar experiment but looked at their feet to step on symmetric targets located next to the treadmill. We tested the LOOK_DOWN group to understand whether direct observation of the feet and treadmill belts rather than a virtual representation of the feet influenced learning. In both INCONGRUENT and LOOK_DOWN, subjects were instructed to walk with nearly equal foot placements, even when the belt speeds became asymmetric. In both of these groups, there was a conflict between the natural adaptation pattern (where the spatial component grows over time) and adherence to the strategy (where the spatial component is near zero). We predicted that this clamping of the spatial component near zero would block the post-learning effects. We also tested whether the subjects implicitly learned the spatial component despite adherence to the strategy

with a 10 second catch trial after 12 minutes of learning. During the catch trial, subjects did not look at their feet, were not given any feedback on the screen, and walked with the 3:1 split in the belt speeds. Following the catch trial, the feedback (either on the screen or by looking at their feet) was restored. Note that the treadmill was stopped briefly between each of these transitions.

Two additional groups (CONGRUENT: n = 10, EXPLICIT_ONLY: n = 10) were tested with visual feedback on the screen that was congruent with implicit learning to investigate whether the visual feedback alone induced any post-learning effects when placed either in concert with implicit learning or in isolation. In these groups, the target locations during the learning phase were based on the foot placements of the IMPLICIT_ONLY's learning phase (averaged across subjects). These target locations were used to ensure that the foot placements in CONGRUENT and EXPLICIT_ONLY changed similarly to IMPLICIT_ONLY over the 15-minute learning phase. CONGRUENT performed the split-belt protocol shown in Figure 3.1B where as EXPLICIT_ONLY performed tied belt walking at 0.5 m/s. This meant that, by the end of learning, both CONGRUENT and EXPLICIT_ONLY demonstrated the same asymmetric foot placement patterns, but only CONGRUENT experienced asymmetric belt speeds.

Statistical analysis

For all groups, we calculated the spatial, temporal, and perturbation contributions as well as the step length difference during late learning (mean of last 30 strides) and initial post-learning (mean of first 5 strides). For INCONGRUENT and LOOK_DOWN, we also measured the mean of the 30 strides leading up to the catch trial and the mean of the strides in the catch trial to measure if the subjects were still learning where to place their feet despite incongruent instruction. ANOVAs or two sample t-tests (when only 2 groups) were used to compare these measures between groups. Post-hoc tests were conducted when appropriate. Decay rates for the spatial component were quantified using 20 epochs of 10 strides for the first 200 strides (with 5 strides in the first bin) similar to Malone and Bastian (Malone and Bastian, 2014). Mixed model repeated measure ANOVAs with epoch as the within-subjects factor and group as the between-subjects factor were used to compare decay rates over time and among groups. All statistical analysis was conducted in Matlab and with an α value < 0.05.

3.2 Results

Post-learning effects in step length difference arise from the spatial component for gradual split-belt learning.

All subjects in this study walked on a split-belt treadmill (Figure 3.1A). One group of subjects (IMPLICIT_ONLY) walked without visual feedback as the right belt speed was gradually increased according to the protocol shown in Figure 3.1B. The step length and foot placement (see Figure 3.1C) was recorded using tracking markers throughout the experiment. Step length difference (fast minus slow) during this walking task can be broken down into spatial, temporal and perturbation components as shown in Figure 3.2 (Finley et al., 2015; Long et al., 2015). To minimize the step length difference during learning, the spatial and temporal components increase to cancel the perturbation component. The spatial and temporal components cancel most of the perturbation, keeping the step length difference within 100 mm on average throughout learning. As in our previous results (Long et al., 2015), we observed that the post-learning effects in step length difference in IMPLICIT_ONLY were due largely to the learning of the spatial component, which only depends on where subjects were placing their feet.

In this experiment, we see after-effects in the difference in step times as seen pre-

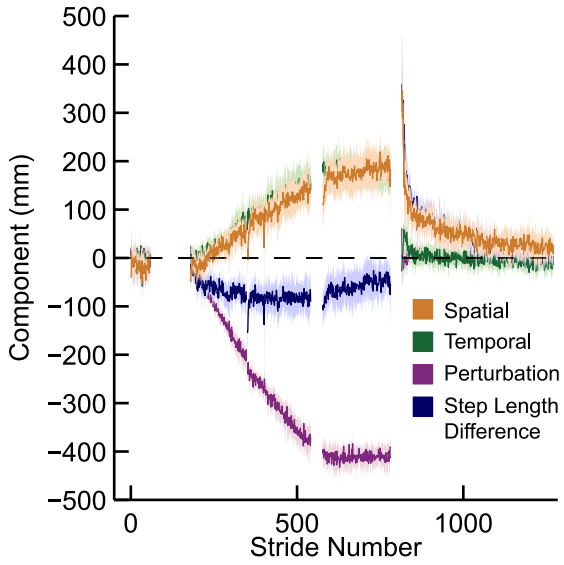

Figure 3.2: Stride-by-stride results (group mean ± 2 SE; in mm) for step length difference, spatial component, temporal component and perturbation component for the IMPLICIT_ONLY group. The number of strides in each phase is cropped to the person with the fewest strides. Note that the learning phase is broken into three 5 minute sections.

viously by Malone and colleagues (Malone et al., 2012). However, when the difference in step times is multiplied by the average belt speed in the temporal component term of the model, the post-learning effects of the temporal component have very small contribution to the step length difference after-effect. Since the temporal and perturbation components contribute very little to the step length difference post-learning effect, we focus our analysis largely on the spatial component (i.e. where subjects are placing their feet).

The spatial component can be clamped through late learning

The step length difference model for the INCONGRUENT and LOOK_DOWN groups are shown with respect to IMPLICIT_ONLY in Figure 3.3 and Figure 3.4, respectively. The subjects in IMPLICIT_ONLY did not receive visual feedback and their foot placements (i.e. spatial component) gradually changed during learning. In contrast, subjects in the INCONGRUENT and LOOK_DOWN groups were instructed to walk with asymmetric step lengths due to symmetric foot placements throughout the learning phase via a feedback display screen (see Figure 3.1A) or by looking at their feet, respectively. Subjects in these groups adhered to the strategy well (74.4 $\pm$2.4 % success for INCONGRUENT), and the spatial component as shown in Figure 3.3B and Figure 3.4B did not grow in late learning as compared to IMPLICIT_ONLY

(ANOVA: $F(2, 27) = 52, p < 0.001$; post-hoc tests: $p < 0.001$ for each group compared to IMPLICIT_ONLY). As a result, the step length difference error grew throughout the learning period and was much greater as compared to the IMPLICIT_ONLY group by the end (ANOVA: $F(2, 27) = 24, p < 0.001$; post-hoc tests: $p < 0.001$ for each group compared to IMPLICIT_ONLY) as shown in Figure 3.3A and Figure 3.4A.

During late learning, we also observed significant differences between groups in the temporal (ANOVA: $F(2, 27) = 6.6, p < 0.01$) and perturbation (ANOVA: $F(2, 27) = 4.2, p = 0.03$) contributions. Post-hoc tests showed that LOOK_DOWN had a higher temporal contribution than INCONGRUENT ($p < 0.01$) and IMPLICIT_ONLY ($p = 0.02$), but no difference between the INCONGRUENT and IMPLICIT_ONLY groups ($p = 0.6$). We also observed that IMPLICIT_ONLY's perturbation was not different than either INCONGRUENT ($p = 0.1$) and LOOK_DOWN ($p = 0.13$), but the perturbation was larger in LOOK_DOWN compared to INCONGRUENT ($p = 0.02$). As a result, it appears that the subjects in LOOK_DOWN increased the temporal contribution as they increased the perturbation contribution, whereas the INCONGRUENT and IMPLICIT_ONLY groups performed both similarly.

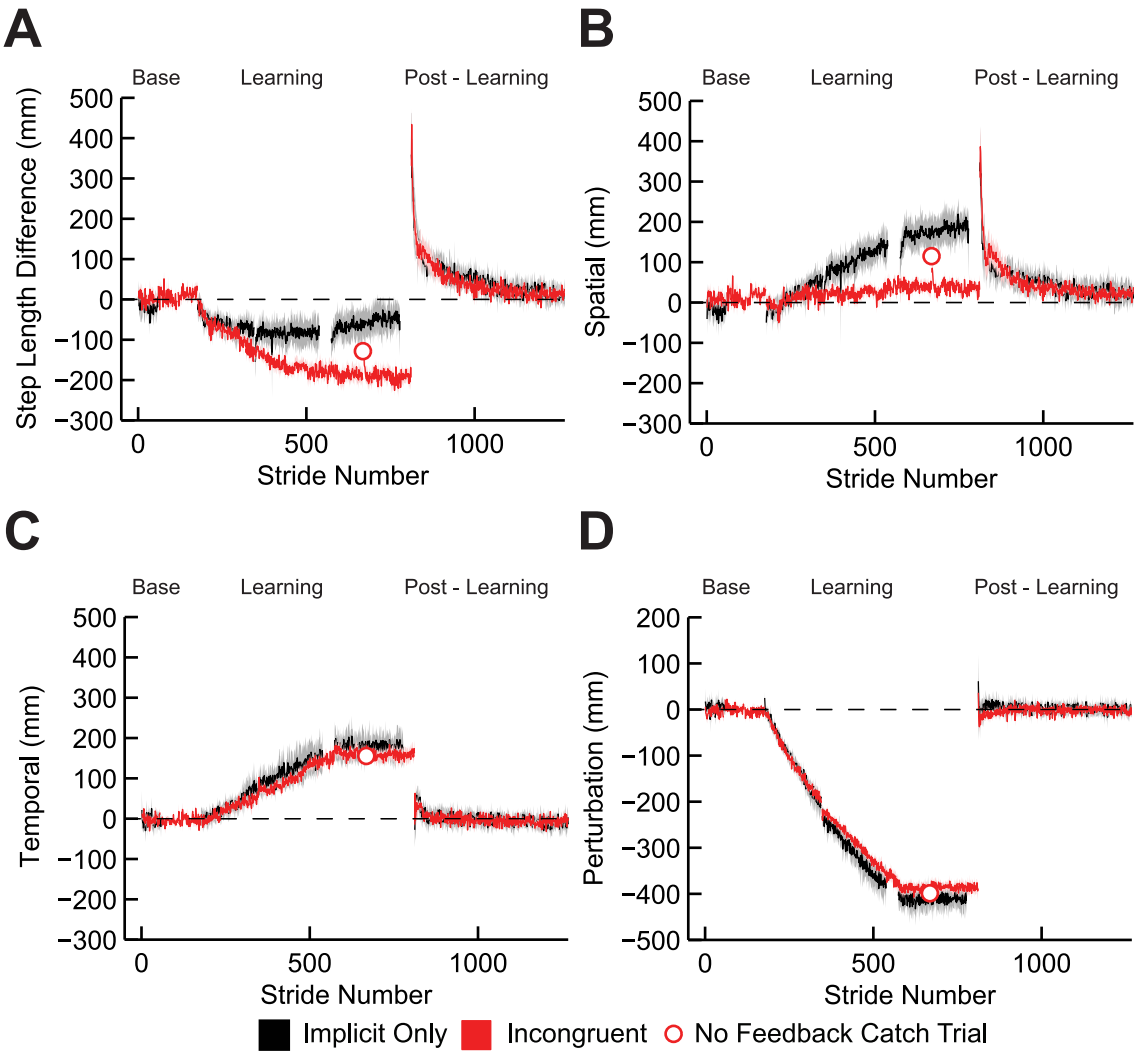

Figure 3.3: Stride-by-stride results (group mean ± 2 SE; in mm) for step length difference (**A**), spatial component (**B**), temporal component (**C**) and perturbation (**D**) component for the INCONGRUENT and IMPLICIT_ONLY groups. The number of strides in each phase is cropped to the person with the fewest strides. Note that the learning phase is broken into three 5 minute sections.

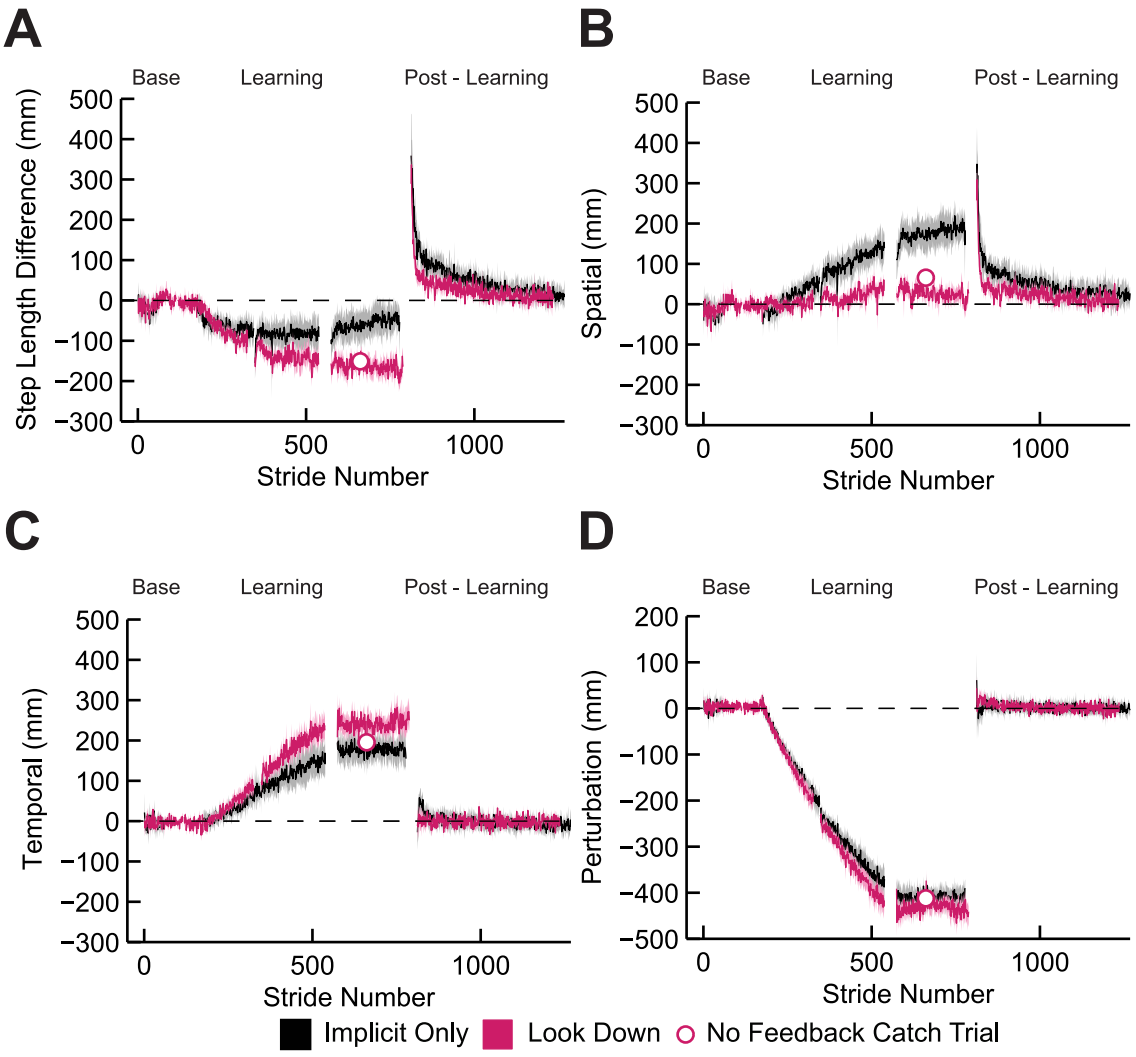

Figure 3.4: Stride-by-stride results (group mean ± 2 SE; in mm) for step length difference (**A**), spatial component (**B**), temporal component (**C**) and perturbation (**D**) component for the LOOK_DOWN and IMPLICIT_ONLY groups. The number of strides in each phase is cropped to the person with the fewest strides. Note that the learning phase is broken into three 5 minute sections.

Clamping the spatial component does not block post-learning effects

We predicted that blocking the expression of spatial learning might eliminate the post-learning step length difference effects. This was not the case — despite showing little change in foot placement during learning, INCONGRUENT and LOOK_DOWN both showed initial post-learning effects similar to IMPLICIT_ONLY (step length difference: $F(2,27) = 1.2, p = 0.32$; spatial: $F(2,27) = 1.8, p = 0.19$; temporal: $F(2,27) = 0.24, p = 0.8$; perturbation: $F(2,27) = 1.6, p = 0.23$). As a result, it appears that forcing subjects to walk with nearly symmetric foot placements and a large step length asymmetry during learning is not sufficient to block the post-learning effects. Similarly, we observed no differences between IMPLICIT_ONLY and INCONGRUENT in the decay of the spatial component (rmANOVA: group effect $F(1,18) = 0.02, p = 0.9$; interaction effect $F(10,180) = 0.7, p = 0.7$). However, we did observe that subjects in LOOK_DOWN had a faster decay as compared to IMPLICIT_ONLY (rmANOVA: group effect $F(1,18) = 4.9, p = 0.04$; interaction effect $F(10,180) = 1.3, p = 0.2$). Thus, it appears that the method of feedback can influence the rate of decay.

To examine if subjects were still learning the spatial pattern during the learning phase, we introduced a catch trial that momentarily removed the feedback while maintaining the split belts. The spatial component immediately jumped to a higher

value in this catch trial for both groups ($p < 0.001$) as shown in Figure 3.3B and Figure 3.4B, but the INCONGRUENT value was higher than the LOOK_DOWN value ($p = 0.03$). Note that these values are lower than the IMPLICIT_ONLY spatial component (both $p < 0.001$), but this may be due to the fact that the treadmill was stopped briefly to turn off the feedback. The immediate jump in the spatial components indicates that the subjects were still learning how to walk on the split-belt treadmill despite the maladaptive incongruent instruction.

Congruent explicit strategy neither enhances nor interferes with implicit learning

The step length difference components for the CONGRUENT and IMPLICIT_ONLY groups are shown in Figure 3.5. Subjects in the CONGRUENT group experienced gradual splitting of the treadmill belt speeds while receiving congruent visual feedback based on IMPLICIT_ONLY's foot placements. This was designed so the explicit strategy was consistent with implicit learning of foot placement (i.e., the instruction guided the subjects to step with the same foot placements that IMPLICIT_ONLY developed naturally during the learning phase). Subjects in CONGRUENT learned a similar gait pattern as IMPLICIT_ONLY by the end of the learning phase (step length difference $p = 0.18$, spatial $p = 0.39$, temporal $p = 0.98$, perturbation $p = 0.49$), indicating that subjects adhered to the instruction (82.6 ± 1.9 % success) and the visual feedback did

not interfere with the learning phase. Furthermore, subjects in CONGRUENT and IMPLICIT_ONLY were similar during the initial post-learning effect (step length difference $p = 0.68$, spatial component $p = 0.87$, temporal component $p = 0.56$, perturbation component $p = 0.85$). Similarly, the spatial contribution decayed at a similar rate for both groups (rmANOVA: group effect $\mathrm{F}(1, 18) = 0.03, p = 0.9$; interaction effect $\mathrm{F}(10, 180) = 0.78, p = 0.6$). Overall, this suggests that explicit instruction in the form of congruent visual feedback does not enhance nor interfere with the automatic post-learning behavior of implicit learning.

Congruent explicit strategy in isolation does not produce post-learning effects

To isolate whether the feedback alone had any effect on post-learning effects, we tested another group of subjects (EXPLICIT_ONLY) with the same visual feedback as CONGRUENT but kept the belt speeds tied at 0.5 m/s. This tied belt walking produced a slower stride time than IMPLICIT_ONLY, and thus reduced the total number of strides taken during the learning phase as can be seen in the stride-by-stride plots in Figure 3.5. Subjects in EXPLICIT_ONLY followed the visual feedback (75.7 ± 1.8 % success) by expressing asymmetric foot placements (i.e. non-zero spatial component) by late learning ($p < 0.001$) despite the tied belts but showed no initial post-learning effects (for non-zero mean: step length difference $p = 0.48$, spa-

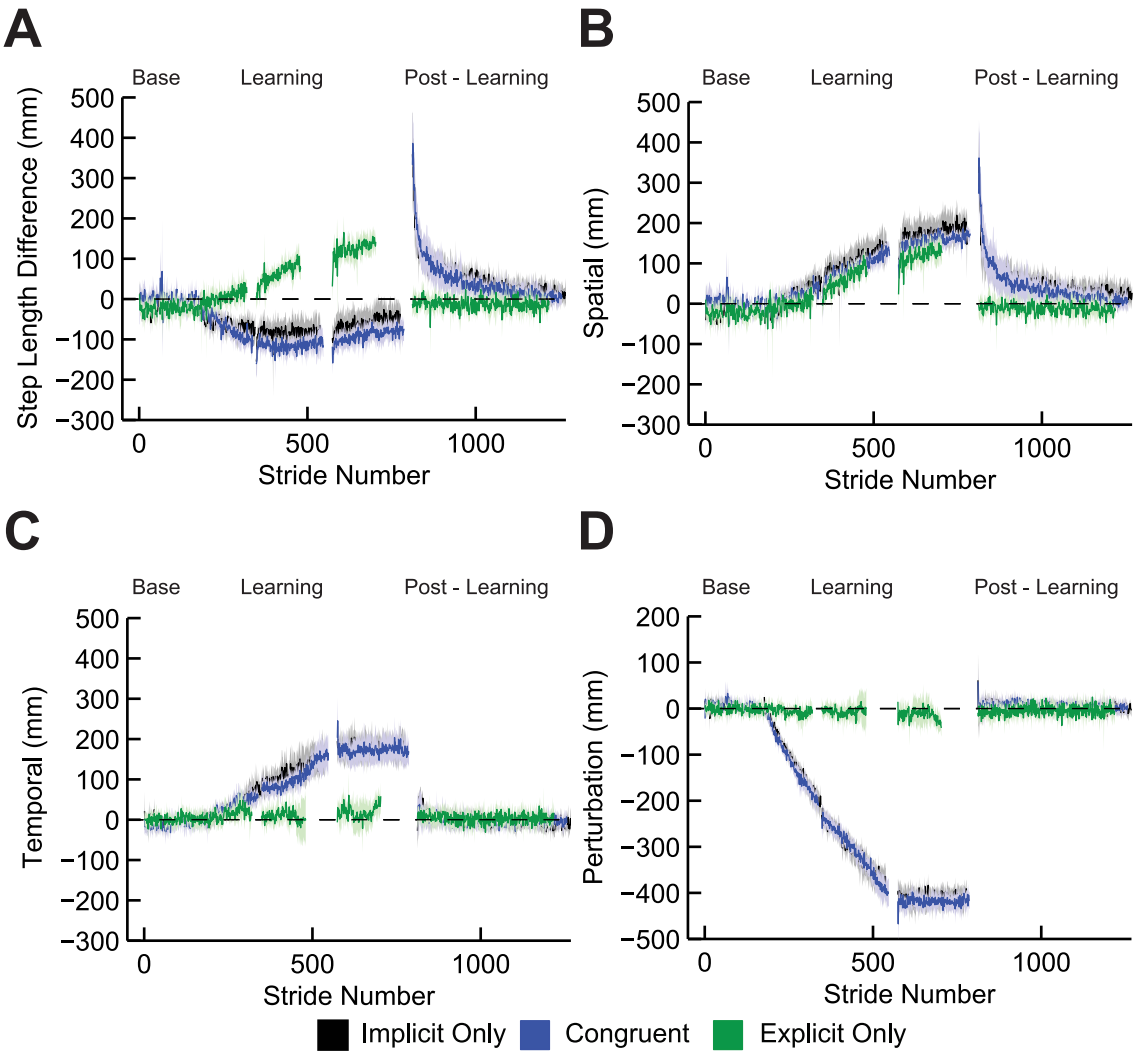

Figure 3.5: Stride-by-stride results (group mean ± 2 SE; in mm) for step length difference (**A**), spatial component (**B**), temporal component (**C**) and perturbation (**D**) component for the CONGRUENT, EXPLICIT_ONLY and IMPLICIT_ONLY groups. The number of strides in each phase is cropped to the person with the fewest strides. Note that the learning phase is broken into three 5 minute sections.

tial component $p = 0.35$, temporal component $p = 0.13$, perturbation component $p = 0.22$). To verify that the number of strides in the learning phase did not influence this result, we conducted a regression with independent variables of group (IMPLICIT_ONLY vs EXPLICIT_ONLY) and number of strides and dependent variable of the initial post-learning effect in the spatial component. This regression revealed that group ($p < 0.001$) was a significant predictor, but number of strides was not a significant predictor ($p = 0.6$). In other words, the fewer strides observed in EXPLICIT_ONLY did not influence this result. More importantly, this results indicates that subjects immediately switched off the explicit strategy when the feedback was removed and they were informed to "do whatever felt natural" in the post-learning phase. This suggests that explicit instruction of new foot placements cannot substitute for the immediate effects of split-belt walking adaptation and has little influence on the post-learning effects observed in INCONGRUENT and CONGRUENT.

3.3 Discussion

Explicit and implicit processes are constantly being used by the nervous system to adjust the walking pattern to changes in the environment. Here, we show that these processes can be used successfully in parallel, and show little interference. Perhaps the most remarkable finding from this work is that the changes in motor output of foot placement during implicit learning need not occur in order for learning to

proceed. Specifically, post-learning effects are surprisingly normal even when an explicit strategy prohibits any change in the motor output during implicit learning. This means that the error (i.e. step length asymmetry) previously thought to drive implicit learning need not be corrected for learning to occur.

Explicit and implicit contributions to motor adaptation have recently been studied in work using visuomotor reaching paradigms. These findings have shown that adaptation can be decomposed into an implicit component and an explicit aiming strategy (Taylor and Ivry, 2011, 2014). An aiming strategy can be acquired with or without instruction and helps subjects to more rapidly counter the perturbation (Mazzoni and Krakauer, 2006; Taylor and Ivry, 2014). However, subjects voluntarily change this explicit aiming strategy over time as they simultaneously learn implicitly from sensory prediction errors (i.e., mismatches between subjects' actual and perceived hand position), even after they have completely counteracted the perturbation (Mazzoni and Krakauer, 2006; Taylor and Ivry, 2014). Thus, in the visuomotor reaching paradigm, explicit and implicit contributions to adaptation interact with one another and work together to recalibrate the motor system. The same visual signal drives these processes, though this signal is compared to different references (e.g. target versus prediction of hand position). These processes will unavoidably interact in learning a new sensorimotor calibration because there is no way to drive them independently. Therefore, it has not been possible to determine whether implicit motor learning depends upon the execution of the recalibrated movements or

can be blocked with an explicit process.

In our work, we were able to investigate the independence of these processes by providing explicit strategy errors based on visual feedback and implicit errors based on proprioceptive signals (Torres-Oviedo and Bastian, 2010). Here subjects can theoretically minimize both error types independently. The INCONGRUENT group showed this behavior as they successfully stepped in the visual target regions (i.e., reduce visual error) and still showed post-learning effects similar to those of IMPLICIT_ONLY. This demonstrates that the explicit and implicit processes operate in parallel with little or no interaction. We show that they operate on different errors since the nervous system is able to build a new predictive model even in the presence of the maladaptive explicit strategy. Similar results have also been seen for subjects who were distracted during a sequence learning task (Seidler et al., 2005, 2002). The distraction prevented improvements in performance during learning, but when the distraction was removed learning improvements were revealed. Our results combined with the sequence learning results provide clear evidence that the nervous system can learn implicitly (i.e. minimize sensory-prediction errors) even if the motor output is not altered during learning.

We also observed a post-learning effect when the spatial component was clamped while subjects looked at their feet, but this effect decayed away more quickly than that of IMPLICIT_ONLY. This effect is similar to that seen when subjects look at their feet during an abrupt split-belt paradigm (Malone et al., 2012). It is likely that

the nervous system is able to predict based on vision the different belt speeds without a sensory-prediction error, which likely limits the construction of a robust internal model.

In this study, we were also interested in understanding if learning shifted to the explicit process when the visual feedback was congruent with implicit learning. Previous work in our laboratory has compared simultaneous implicit and explicit learning during walking, though with a different type of paradigm (Malone and Bastian, 2010). Those subjects were exposed to an abrupt split in the treadmill belts and were instructed to equalize their step lengths using video feedback of their legs. Video feedback induced faster learning, but no difference in the post-learning effects (i.e. size and rate of washout) compared to a control group. Since the learning rates differed between groups, the effect of the explicit process on the post-learning phase is unclear as previous work in reaching showed that the rate of learning also influences the rate of washout (Huang and Shadmehr, 2009).

Here we hypothesized that providing visual feedback congruent with the rate of implicit learning could interfere with post-learning effects (Benson et al., 2011; Malone and Bastian, 2010; Wulf and Prinz, 2001). Subjects may rely more on the visual feedback, and thus learn less through the implicit process (Schmidt, 1991). Contrary to our hypothesis, subjects with congruent visual feedback during gradual learning showed similar post learning effects (i.e. size and rate of washout) compared to a control group with no visual feedback. This suggests that explicit control of walking

neither interferes with nor enhances the post-learning effects of implicit learning.

As a control experiment, we were also interested in understanding whether explicit instruction in isolation influences post-learning effects. We had hypothesized that we may see a small effect due to use-dependent plasticity (Diedrichsen et al., 2010; Verstynen and Sabes, 2011) but this was not the case following 15 minutes of isolated explicit instruction. This result is similar to a reaching experiment that had subjects use an explicit strategy when aiming at a target with veridical feedback. This work showed that subjects had no difficulty abruptly switching between explicit strategies, which resulted in no post-learning effects (Mazzoni and Krakauer, 2006). As a result, it is possible that subjects were relying on the feedback to produce the asymmetric foot placements in our explicit instruction experiment and therefore did not have to recalibrate their automatic walking patterns.

The cerebellum has long been considered the site of implicit error-based learning as patients with cerebellar damage show impairments in adaptation to split-belt walking (Morton and Bastian, 2006), throwing with prisms (Martin et al., 1996; Weiner et al., 1983), force-field reaching (Rabe et al., 2009; Smith and Shadmehr, 2005), and visuomotor rotation reaching (Gibo et al., 2013; Izawa et al., 2012; Rabe et al., 2009; Taylor et al., 2010). However, neural circuits involved in explicit motor learning are still unknown. Recently, Taylor et al. instructed patients with cerebellar damage to use an explicit strategy to successfully cancel a visuomotor rotation; they were able to do this but did not show post-learning effects (Taylor et al., 2010). This same ex-

perimental paradigm was then repeated with patients with prefrontal cortex lesions, who had difficulty following the explicit strategy but showed post-learning effects (Taylor and Ivry, 2014). This double dissociation suggests that the explicit strategy depends on prefrontal cortex. Other studies of patients with prefrontal cortex lesions demonstrated that these patients have reduced explicit awareness and impairments in learning (Beldarrain et al., 1999; Slachevsky et al., 2001, 2003; Taylor and Ivry, 2014). This idea of the prefrontal cortex as an important site involved in explicit learning is further supported by work in neuroimaging, which indicates that the prefrontal cortex is active during sensorimotor adaptation (Floyer-Lea and Matthews, 2004, 2005; Sakai et al., 1998; Shadmehr and Holcomb, 1997). Therefore, it is possible in our walking experiments that the prefrontal cortex uses visual error to update an explicit strategy, whereas the cerebellum uses sensory prediction error to update the implicit internal model.

In summary, our experiments with explicit learning via visual feedback and implicit learning via a split-belt treadmill provide clear evidence that the explicit and implicit learning processes are independent, depend on different error signals and operate in parallel in the central nervous system.

Acknowledgements

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Chapter 4

Sensory cancellation in human locomotor learning

Walking generally requires little conscious focus for both stable perception and accurate movement. Consider what happens when you step onto an icy walkway- you must accurately perceive the environment and then use this information to adapt your walking to stay upright. It has been suggested that some gait dysfunction (e.g. asymmetric step lengths) may result from the inability of a damaged nervous system to properly perceive, and then correct, these abnormalities (Wutzke et al., 2015). Dysfunction in proprioceptive perception has been observed in several populations with neurological damage, including cerebral stroke (Connell et al., 2008) and cerebellar damage (Bhanpuri et al., 2013). Therefore, improving the ability of patients' perception through rehabilitation provides a promising approach for enabling the ner-

vous system to naturally correct movement disorders. However, the design of such rehabilitation strategies requires thorough understanding of how and why perceptual changes can occur.

Our perception of the world depends on the sensory signals that our nervous system is receiving. These sensory signals are from both the surrounding environment and from feedback resulting from initiated movement (Blakemore et al., 1998; Cullen, 2004). In order to properly maintain calibration of both the motor and sensory systems, the nervous system must distinguish between these two types of signals. Sensory cancellation, where expected sensory consequences of motor actions are canceled from the incoming sensory signal (Holst and Mittelstaedt, 1950), is one proposed mechanism that allows for distinguishing environmental versus feedback signals. Evidence in support of this theory has been observed in many systems, including the weakly electric fish electrosensory system (Bell, 2001), the primate vestibular system (Cullen, 2004) and the human tactile system (Blakemore et al., 1998). However, it remains unknown if sensory-cancellation contributes to 1) human locomotion and 2) motor learning processes.

We studied people walking on a split-belt treadmill with one belt moving faster than the other. Prior to split-belt walking, subjects do not expect the belt speeds to differ. While walking with split belts, subjects develop an expectation that one belt will be moving faster than the other. When the belts are returned to the same speed, subjects express both a motor after-effect (unequal steps) (Long et al., 2015;

Reisman et al., 2005) and a perceptual after-effect (reporting that the previously slow belt is now faster) (Jensen et al., 1998; Reisman et al., 2005; Vazquez et al., 2015). We hypothesized that the perceptual after-effect is caused by the continued expectation of different treadmill belt speeds, which then cancels a portion of the incoming sensory signal.

To evaluate this sensory-cancellation hypothesis, we designed a multi-phase experiment to measure speed perception and to estimate subjects' speed expectations. We then determined if subjects' speed perception could be predicted by subtracting their speed expectations (generated from their movement) from the actual treadmill belt speeds. The results presented here show clear evidence that a sensory cancellation mechanism can explain the perceptual after-effects observed after locomotor learning. It further suggests that perceptual and motor learning both depend on expectations of the environment and provides new insights into how the human sensorimotor system operates during locomotion.

4.1 Methods

Subjects

16 healthy adults (11 females, age range 18-36) completed the multi-phase protocol shown in Figure 4.1A. All subjects gave informed consent before participating. The protocol was approved by the Johns Hopkins Institutional Review Board.

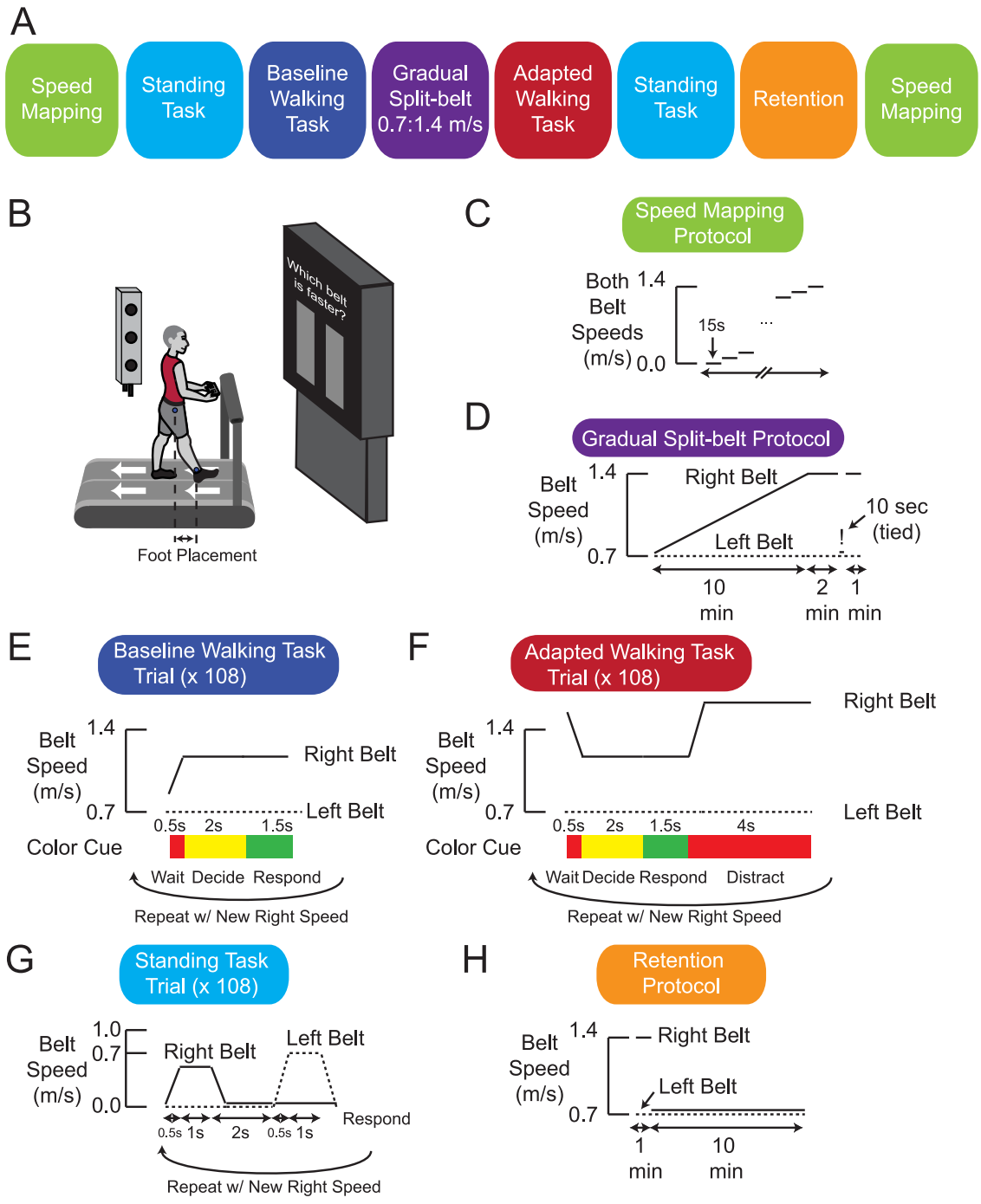

Figure 4.1: Caption next page.

(Previous Page.) Perceptual learning protocol. (**A**) Overall protocol. (**B**) Subjects walked on a split-belt treadmill. During perception tasks, subjects held a two-button keypad for indicating which belt was faster. (**C**) Speed mapping protocol: subjects walked at a range of tied-belt speeds to record normal walking parameters. (**D**) Gradual split-belt protocol: the right belt speed was gradually increased to induce locomotor learning. A 10 second catch-trial was inserted to measure motor after-effects (**E**) Baseline walking task: one trial of the baseline two alternative forced-choice task, in which subjects reported which belt was faster while walking. (**F**) Adapted walking task: one trial of the adapted task. (**G**) Standing task: one trial of the task in which one belt moved at a time. (**H**) Retention protocol: subjects walked at the full split and then washed out, in order to measure de-adaptation.

Data collection

Subjects walked on a split-belt treadmill (Woodway), a treadmill with one belt for each foot (Figure 4.1B), occasionally with the belts moving the same speed ("tied belts") and other times with the belts moving at different speeds ("split-belts"). The treadmill belts were controlled with custom-software (Vizard, World Viz). Infrared-emitting markers were placed bilaterally over the lateral malleolus and greater trochanter. The three-dimensional marker positions were recorded at 100 Hz with an Optotrak (Northern Digital) motion capture system. Force plates located under each treadmill belt collected vertical forces at 1000 Hz. These forces were utilized to compute heel strike events. Occasionally, subjects held a two button keypad for use with perception tasks (see Figure 4.1B).

Experimental set-up

For safety purposes, subjects wore a non-load bearing harness attached to the ceiling. A thin divider was placed between the belts to prevent stepping on the opposite treadmill belt. Prior to starting and stopping the treadmill belts, subjects held onto a handrail located in front of the treadmill. Immediately after the belts started moving, subjects let go of the handrail. To prevent blocking the tracking markers, subjects were instructed to either cross their arms or hold onto the keypad in front of their body. For the sections of the experiment that did not include a perceptual task, subjects watched a self-selected movie on a TV screen in front of them.

Speed mapping

At the beginning and ending of the experiment, subjects walked on the treadmill for a range of tied-belt speeds in order to measure normal baseline walking behavior. Subjects began by marching in place with the belts not moving. After 15 seconds, the belts turned on at 50 mm/s. The speeds were then increased every 15 seconds by 50 mm/s until 1400 mm/s (Figure 4.1C).

Gradual split-belt adaptation

The adaptation portion of the experiment consisted of gradually increasing the right treadmill belt from 700 mm/s to 1400 mm/s over a period of 10 minutes while holding the left treadmill belt constant at 700 mm/s (Figure 4.1D). This section also contained a 10 second catch trial with the belts both moving at 700 mm/s to measure motor learning after-effects. The treadmill was stopped momentarily before and after the catch trial.

Walking perception task

Subjective speed perception between limbs using a two-alternative forced choice task. Subjects were asked which treadmill belt felt faster for a range of speed differences, while subjects were walking with both belts moving simultaneously. This task was completed before and after the gradual split-belt adaptation protocol. The left treadmill speed was always at the reference speed of 700 mm/s and the right treadmill speed varied on each trial (Figure 4.1E). A visual display placed in front of the treadmill changed colors to cue the subjects about different parts of the trial. A trial began with a red screen in which the treadmill belts were accelerating to the desired test speeds. After 0.5 seconds, the screen turned yellow to cue the subjects to figure out which belt was faster during that segment. Subjects had 2 seconds to make this decision before the screen turned green. The green screen cued the subjects

to push a button on the keypad corresponding to which belt was faster during the yellow period. The test speed was maintained during this green period, but subjects were instructed to push the button as soon as they saw the green cue. If the subjects did not respond in a 1.5 second window the trial was discarded. When the subjects pushed the button, the screen turned red indicating that their response was recorded. The baseline task used the method of constant stimuli with each speed difference presented 12 times. The right belt speed varied in a random order (400, 500, 600, 700, 750, 800, 900, and 1000 mm/s). Occasionally additional trials were added in the baseline period to improve psychometric fits.

The adapted version of this task (Figure 4.1F) was based on an adaptive psychometric technique originally proposed by Watt and Andrews (Watt and Andrews, 1981). Since prior work has demonstrated that the set of stimuli should be centered on the 50% response criteria (Wichmann and Hill, 2001b), this psychometric technique was used instead of the method of constant stimuli because the bias and sensitivity varied significantly among subjects and thus a fixed set of stimuli was not appropriate for all subjects. An adaptive staircase procedure also was not used because we were interested in estimating both the entire psychometric function, which is difficult to accomplish in a staircase (Leek, 2001). This adapted task consisted of four blocks of stimuli with a total of 118 trials. The first block presented a range of speeds (900 : 100 : 1400 mm/s) four times in a random order to determine a rough approximation of the perceptual equivalence speeds, the right belt speed that subjects report

as equal to the left belt speed. The remaining three blocks consisted of presenting five stimuli speeds six times each in a random order. The stimuli speeds for the right belt were selected from a speed set (800 : 50 : 1600 mm/s) with two below, two above and one at the approximate perceptual equivalence speed. After each block, all data was used to estimate a new perceptual equivalence speed. The spread of the stimuli was selected by the experimenter based on how the subject was performing the task (i.e. subjects with high sensitivity had a smaller range than subjects with lower sensitivity). All blocks began with a right test speed at 700 in order to monitor deadaptation.

Prior work has shown that when subjects experience a random perturbation of split-belt speeds they adapt to the mean split (Torres-Oviedo and Bastian, 2012). Therefore, to prevent deadaptation during the adapted task, each test speed was followed by a distractor speed for 4 seconds (Figure 4.1F). The distractor speeds and the test speeds averaged out to 1400 mm/s (the desired split level). The order of the distractor speeds was also randomized to minimize the occurrence of very large jumps in the treadmill speeds. Subjects were not required to report which belt was faster during the distractor speeds, so the visual displayed remained red.

Standing perception task

Another method for measuring speed perception is to present one speed at a time on each side of the body while the other treadmill belt was stationary (Figure

4.1G). This two alternative forced choice task was also completed before and after adaptation. Each treadmill belt accelerated for approximately 0.5 seconds and was held constant for 1 second before coming to a stop. There was a 2 second delay between each belt moving to allow for subjects to place their foot in front of them. Subjects reported their response with a keypad after feeling each belt move. The baseline and adapted task both used the method of constant stimuli with each speed difference presented 12 times. The left belt was always the reference speed at 700 mm/s and the right belt speed varied in a random order (400, 500, 600, 650, 700, 750, 800, 900, 1000 mm/s). Half of the trials began with the left belt moving first and the other half began with the right belt moving first in a blocked manner (54 trials each). The side of the first belt moving was counterbalanced across subjects and the opposite side was used for the first block in the adapted task. Occasionally, additional trials were added with a finer range of speeds (600 : 25 : 800 mm/s) for subjects with high sensitivity in the baseline task. For these subjects, the finer speed range was used for the adapted task.

Retention

After completing both adapted perception tasks, subjects walked with the full split (700:1400 mm/s) for 1 minute to measure retention of the split pattern following the standing task and then walked with both belts tied at 700 mm/s for 10 minutes to wash-out the aftereffects (Figure 4.1H).

Data analysis

Here, foot placement is defined as the anterior-posterior distance between the average hip marker and the ankle at heel strike. Step time is defined by the time between heel strike of opposite sides of the body. The slow step time begins with heel strike on the slow belt and ends with heel strike on the fast belt. To account for different step times, the normalized foot placement is defined as foot placement divided by step time (e.g. slow foot placement divided by slow step time). A linear regression was performed to create a mapping between treadmill belt speed and normalized foot placement. This mapping allows us to predict the expected treadmill speed based on normalized foot placement.

For each psychometric task in this experiment, a psychometric function $\Psi(x)$ based on the equation

$$\Psi(x;\mu,\sigma,\gamma,\lambda) = \gamma + (1-\lambda-\gamma)F(x;\mu,\sigma) \tag{4.1}$$

was fit using a constrained maximum likelihood method with the Matlab version of Psignifit 3.0 (Fründ et al., 2011). Here, $F(x;\mu,\sigma)$ is the normal cumulative distribution function with mean μ and standard deviation σ at stimulus speed x. The other two parameters (λ and γ) represent upper and lower lapse rates respectively to account for subjects incorrectly responding regardless of the test stimulus level (Wichmann and Hill, 2001b). Goodness of fit was based on the deviance (log-likelihood ratio) of

2000 boot strap samples. For a full description of this metric see the extensive work by Wichmann and Hill (Wichmann and Hill, 2001b). 2 subjects were removed from the analysis for deviance values that exceeded the 95 percent confidence of the boot strap samples. The bias (50% threshold) and just-noticeable difference (75% minus 50% thresholds) were calculated for each task for each subject. The central 95 percent confidence intervals for these parameters were determined using 2000 parametric bootstrapped samples (Wichmann and Hill, 2001a).

To test the sensory-cancellation hypothesis, we created a predicted psychometric curve based on how subjects were walking in each of the walking perception tasks. The procedure for creating this predicted curve is as follows. For a given speed difference ΔS, we locate all steps within the task that occurred at that speed difference (n total steps). The measured normalized foot placements for each of these n steps were then converted into expected speeds (ΔE) using the linear relationship described above. Then, we estimate n perception speed differences as

$$\Delta P = \Delta S - \Delta E \tag{4.2}$$

which indicates that we predict the subjects perception as the expected speed difference subtracted from the actual speed difference. Using all steps for a given speed difference, we calculate the probability that this perception difference is greater than

zero with

$$Prob(\Delta P > 0; \Delta S) = \frac{\#\Delta P > 0}{n} \tag{4.3}$$

where the numerator indicates the number of times ΔP is greater than zero for a given speed difference ΔS. This gives us the predicted probability of reporting the right belt as greater than the left as a function of belt speed difference. A new psychometric function is then fit to these predicted probabilities. If the sensory-cancellation theory holds, the predicted psychometric functions should match the measured psychometric functions.

All statistical tests were conducted in Matlab and statistics were considered significant for $p < 0.05$.

4.2 Results

Expected sensory consequences based on foot placement adapt during split-belt walking

We estimated subjects' expected treadmill belt speeds based on where they placed their feet. Subjects stepped farther forward for faster speeds in baseline walking conditions. Since prior work has demonstrated that changes in stepping cadence also alter foot placement (Hussain et al., 2013), we normalized foot placement to the step time (time between heel strikes of opposite legs). As shown for a representative subject

in Figure 4.2A, we observed that normalized foot placement has an approximately linear relationship with treadmill belt speed ($R^2 > 0.94$ for each leg for all subjects). As a result, we use this linear relationship to estimate the brain's expected speed based on each normalized foot placement throughout the experiment.

To induce locomotor learning and change subjects' speed expectations, subjects completed a gradual split-belt protocol, in which the left belt speed was fixed at 700 mm/s while the right treadmill belt speed gradually increased from 700 mm/s to 1400 mm/s over a period of 10 minutes. Results showed that subjects adapted the expected speed difference (right minus left) based on the normalized foot placement and exhibited aftereffects in a tied-belt catch trial following learning as shown in Figure 4.2B. These results validate that subjects develop an expectation during learning that the slow belt should be slower.

Walking adaptation biases speed perception

It was observed that the expected speed difference was less than the actual speed difference, indicating that the perception of the belt speed difference also adapted. To measure this change in perception, subjects completed a two-alternative forced choice speed perception task before and after adaptation while walking that required subjects to report which belt was faster for a range of belt speed differences. The probability of reporting the right belt speed as greater than the left belt speed for a range of speeds is shown in Figure 4.3A for a representative subject. A psychometric

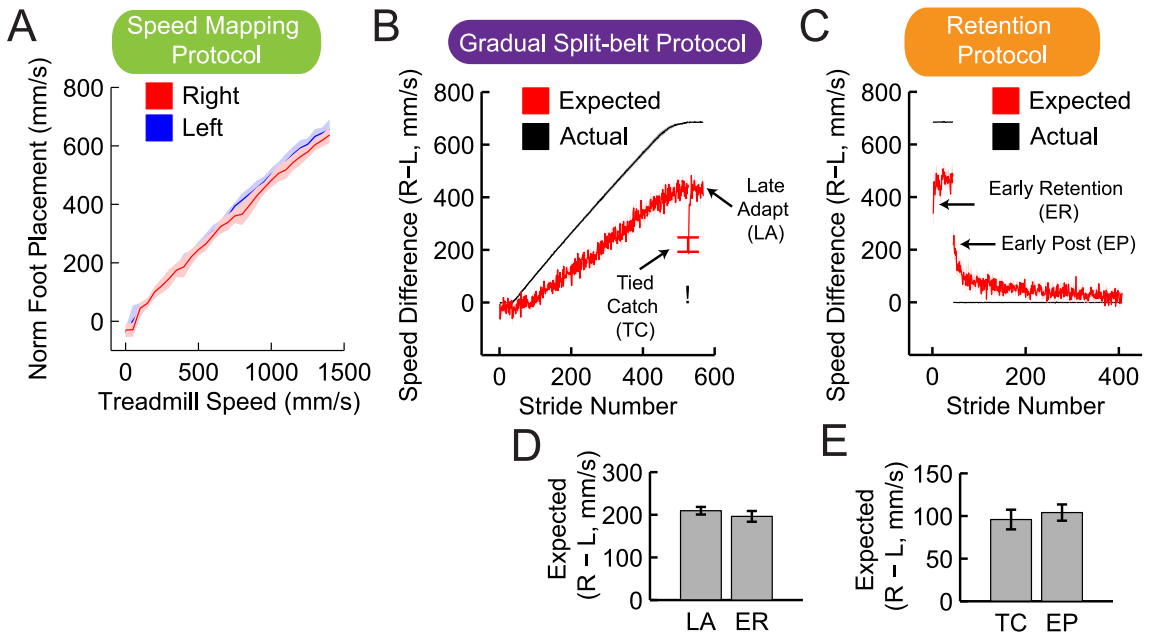

Figure 4.2: Speed Expectation Results. (**A**) Normalized foot placement (foot placement divided by step time) for a range of treadmill speeds for a representative subjects as measured in the speed mapping protocol (see Figure 4.1C). (**B**) The speed difference (right minus left) during the gradual split-belt protocol (see Figure 4.1D) for the actual difference and the expected difference. (**C**) The speed difference (right minus left) during the retention protocol (see Figure 4.1H) for the actual difference and the expected difference. (**D**) The expected speed difference for late adaptation (LA) and early retention (ER). (**E**) The expected speed difference for the tied-catch (TC) trial and early post-adaptation (EP).

function (see Equation 4.1 in Methods) was fit to each set of psychometric data and then the bias (50% threshold) and the just noticeable difference (JND, difference between the 75% and 50% thresholds) were calculated for the baseline and adaptation tasks. After adaptation, subjects showed a significant increase in bias ($p < 0.001$) as shown in Figure 4.3B, which indicates that they felt the belt speeds were equal when they were in fact drastically different. Furthermore, subjects were also more uncertain of their responses as indicated by an increase in the JND ($p < 0.001$) as shown in Figure 4.3C. These results indicate that subjects adapt their perception as well as their action during walking on a split-belt treadmill, as also supported by previous split-belt work (Jensen et al., 1998; Reisman et al., 2005; Vazquez et al., 2015).

Adaptation does not bias speed perception during standing

Another method for testing a subject's speed perception is to have only one treadmill belt move at a time while the other treadmill belt is stationary. Subjects completed this standing perception task before and after adaptation by again asking them to report which of the two sequential belt speeds was faster in a two-alternative forced choice manner. The psychometric data and fitted psychometric functions for these tasks for the same representative subject are shown in Figure 4.4A. In this task,

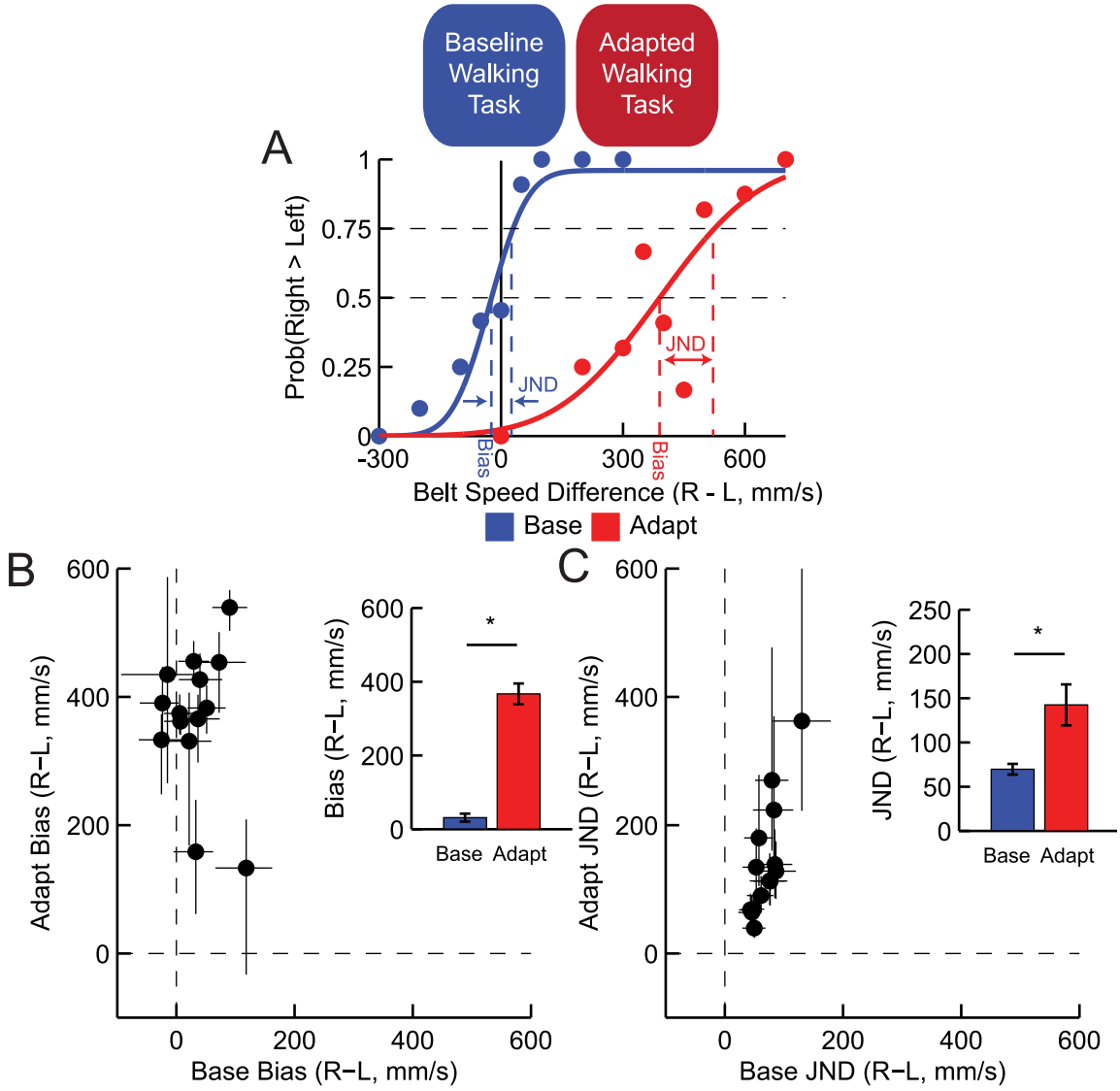

Figure 4.3: Walking Perception Tasks. Subjects completed two alternative-forced choice tasks (see Figure 4.1E and Figure 4.1F) to indicate which belt speed was faster for a range of speed differences while both belts moved at the same time. The left belt speed was always at 700 mm/s and the right belt speed was varied. (**A**) The probability of reporting the right belt speed as greater than the left belt speed for the baseline task (blue) and after adaptation (red) for a representative subject. Psychometric functions were fit to each task's perceptual data and the bias and just noticeable difference (JND) were estimated. (**B**) The bias for the baseline and adaptation tasks (with 95% bootstrapped confidence intervals) for each subject. The inset shows that following adaptation subjects have a greater bias than baseline. (**C**) The JND for the baseline and adaptation tasks (with 95% bootstrapped confidence intervals) for each subject. The inset shows that subjects also had a higher JND after adaptation.

subjects showed in general no difference between adaptation and baseline in the bias ($p = 0.10$) or just noticeable difference ($p = 0.12$) as shown in Figure 4.4B and Figure 4.4C, respectively. This indicates that locomotor learning on the split-belt treadmill does not induce a global sensory change but rather a perceptual change that is context-specific to the act of walking.

To test if subjects deadapted during the standing task, subjects completed a retention protocol. This protocol began with 1 minute of split-belt walking followed by 10 minutes of tied-belt walking. The expected speed differences (based on normalized foot placements) for this protocol are shown in Figure 4.2C. Results indicate that subjects did not deadapt during the perception tasks because we observed (1) no differences between late adaptation and early split-belt retention ($p = 0.18$, see Figure 4.2D) and (2) no differences between the tied-belt catch trial and early post-adaptation ($p = 0.4$, see Figure 4.2E). These results reveal that the nervous system is still capable of sensing the difference between the belt speeds in the adapted state, but that the act of walking ultimately influenced the perception.

Biased speed perception is predicted by a sensory-cancellation model

Using the actual speed difference and the expected speed difference based on kinematics of normalized foot placement, we can make a prediction about each subject's

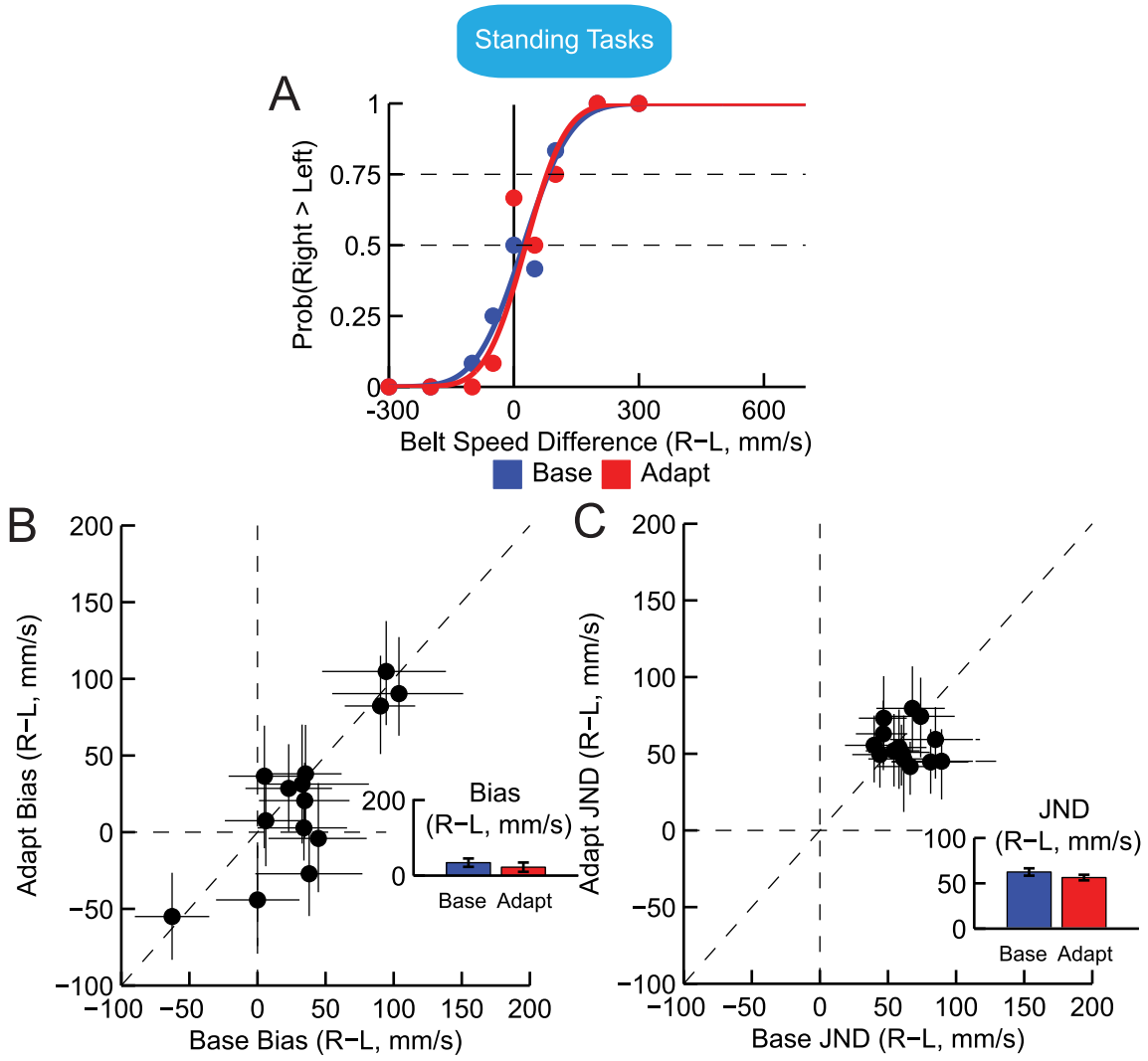

Figure 4.4: Standing Perception Tasks. Subjects completed two alternative-forced choice tasks (see Figure 4.1G) where only one belt moved at a time and they reported which speed was faster. (**A**) The probability of the reporting the right belt speed as greater than the left belt speed for a representative subject is shown as a function of the right belt speed with a fixed left belt speed. Psychometric functions were fit to each subject's perceptual data and the bias and just noticeable difference (JND) were estimated. (**B**) The bias for the baseline and adaptation tasks (with 95% bootstrapped confidence intervals) for each subject. The inset shows that there was no difference in the bias before and after adaptation. (**C**) The JND for the baseline and adaptation tasks (with 95% bootstrapped confidence intervals) for each subject. Similarly as shown in the inset, there was no difference in the JND from baseline to adaptation.

psychometric function using a predicted perception approximated by actual minus expected (Figure 4.5A for the representative subject). These perception predictions are based on calculating the fraction of steps for a given speed difference that have actual minus expected as greater than zero and dividing by the total number of steps. Psychometric functions are then fit to these predicted perception probabilities. Our data show that we can successfully predict the adaptation psychometric functions with similar precision to the baseline psychometric function for the bias ($p = 0.82$, Figure 4.5B) and just noticeable difference ($p = 0.43$, Figure 4.5C). These results provide clear evidence that the perceptual after-effect observed during the walking perception task depends on sensory-cancellation in which the expected sensory consequences due to the motor after-effect were canceled (i.e. subtracted) from the incoming sensory signal.

4.3 Discussion

Sensory cancellation and locomotor learning

Following adaptation to walking on a split-belt treadmill with one belt moving faster than the other, subjects developed an expectation that one belt would be faster than the other, which was revealed by motor aftereffects when the split-belt perturbation was removed. In addition, subjects completed perception tasks before and after adaptation in which they reported which treadmill belt was faster for a range of speed

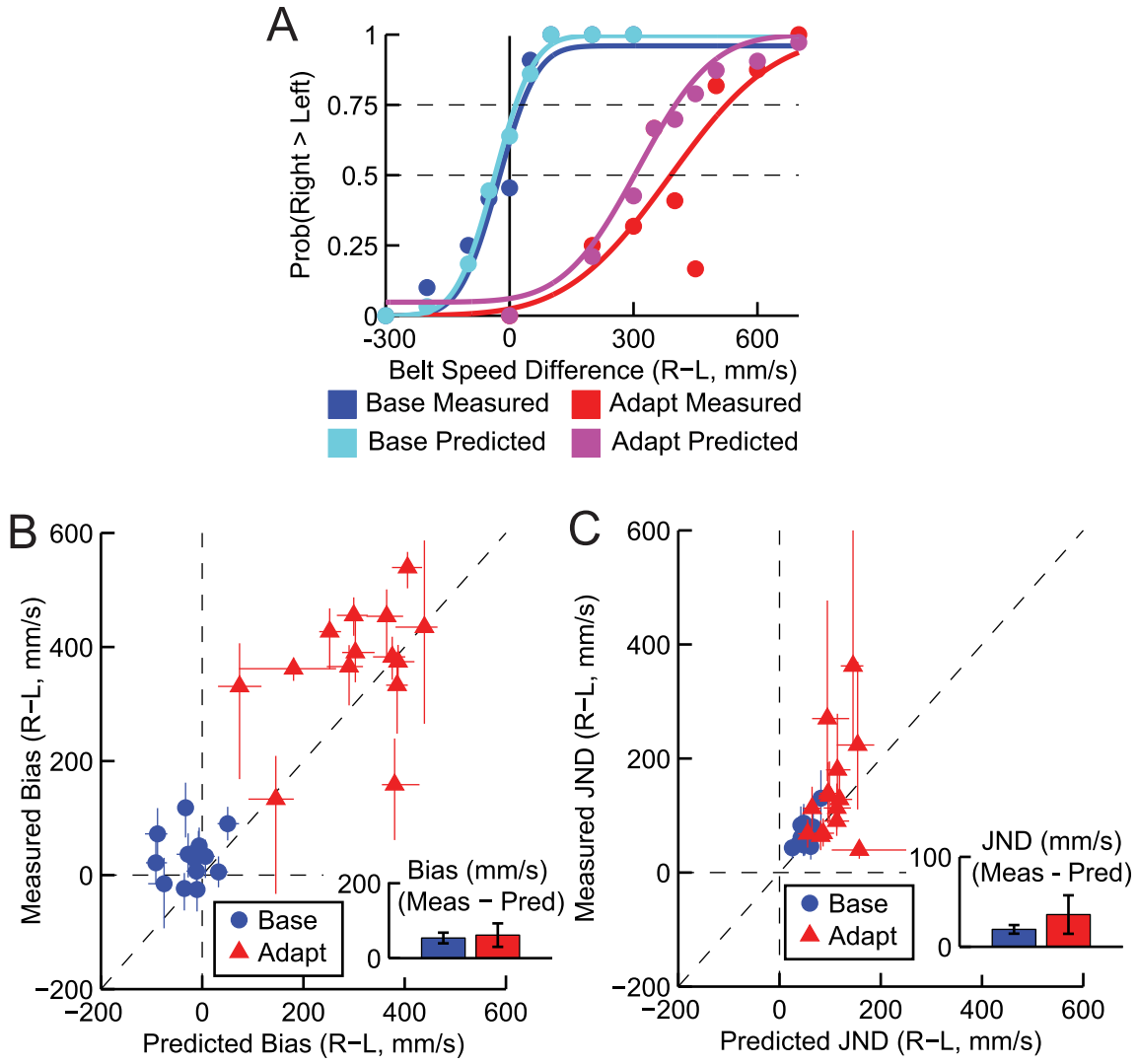

Figure 4.5: Predictions of Walking Perception Tasks. The sensory-cancellation model (i.e. perception = actual - expected) was used to predict the psychometric functions for each individual subject. The expected speed difference was estimated using normalized foot placement. (**A**) The predicted and measured psychometric functions for the baseline and adaptation walking tasks for a representative subject. (**B**) The predicted and measured bias (with 95% bootstrapped confidence intervals) for each individual subject for the baseline and adaptation walking tasks. The inset shows no bias difference between baseline and adaptation in the difference in measured and predicted. (**C**) The predicted and measured just noticeable difference (JND; with 95% bootstrapped confidence intervals) for each individual subject for the baseline and adaptation walking tasks. The inset shows no JND difference between baseline and adaptation in the difference in measured and predicted.

differences. In general, we observed no changes in perception for the standing version of this task, suggesting that the nervous system's ability to sense the difference in speeds was preserved. On the other hand, during the walking task subjects reported that the belts were equal after adaptation when they were drastically different, suggesting a change in their perception of the world during active movement. Similar shifts in localization perception have also been observed following upper-limb adaptation reaching protocols (Cressman and Henriques, 2009; Haith et al., 2009; Mattar et al., 2013; Ostry et al., 2010), indicating that perception after-effects are common artifacts of motor adaptation.

These locomotor findings are consistent with the sensory-cancellation theory originally proposed by Von Holst and Mittelstaedt (Holst and Mittelstaedt, 1950). In their theory, the nervous system can improve its perception of the world by eliminating the expected sensory consequences of an action. Here, the speed perception following adaptation was significantly biased during walking due to incorrect expectations as revealed by motor aftereffects. This sensory-cancellation phenomenon appears to be a general mechanism as it has been conserved across many species including weakly electric fish (Bell, 2001), primates (Cullen, 2004) and humans (Blakemore et al., 1998).

The data presented here is closely associated with the work in the primate vestibular system (Angelaki and Cullen, 2008; Roy and Cullen, 2004) as both locomotor and vestibular neural circuits are thought to be mostly subcortical. In prior work, Roy and Cullen demonstrated through single-cell recordings that vestibular neurons respond

differently for active and passive head movements (Roy and Cullen, 2004). Brooks and colleagues have extended this research to the learning domain by introducing a perturbation with a torque to the primate's head during active movements (Brooks et al., 2015). Based on our work, we hypothesize that primates are experiencing a shift in perception when the torque perturbation is removed. Given our work was performed with human subjects, and thus does not include neural recordings; we are able to assess both perception and motor action simultaneously during locomotor learning.

The cerebellum and its importance for sensory-cancellation

The most well studied system with sensory-cancellation is likely the electrosensory system of sharks and weakly electric fish (Bell, 2001). These species use their electrosensory system to detect the location of nearby prey. It is important for these species to apply sensory cancellation as their own movements and active generation of electric signals (for weakly electric fish) produce changes in the electric field. Prior work has demonstrated that their sensory cancellation is dependent on cerebellar-like areas (Bell, 2001). In higher species such as the primate, the vestibular system is accounting for active head movements (i.e. sensory-cancellation) via the cerebellum (Brooks et al., 2015; Roy and Cullen, 2004). The cerebellum has also been implicated

in the human nervous system as fMRI signals show different signal strengths in the cerebellum for self-generated versus externally-generated tactile stimulation (Blakemore et al., 1998). These differential cerebellar signals then produce different signal strengths of somatosensory cortex, the site of human tactile perception, indicating why you cannot tickle yourself (Blakemore et al., 1998). Together, these results reveal that the cerebellum is likely involved in the sensory-cancellation mechanism.

Prior theoretical and experimental work has suggested that the cerebellum is well equipped to predict the sensory consequences of a movement through a feedforward internal model (Shadmehr and Mussa-Ivaldi, 1994; Wolpert et al., 1995). When a motor action is generated, an 'efference copy' of the movement is likely transmitted to the cerebellum. The output of this forward model can then be compared to the actual sensory signal. The difference between the expected and actual signals has been termed the sensory-prediction error (Shadmehr and Mussa-Ivaldi, 2012; Wolpert et al., 1995), which can be used to update the forward model as well as to modify future motor actions.

It is likely that the sensory-cancellation observed here is dependent on the cerebellum as prior work has shown that patients with extensive cerebellar damage do not adapt and do not show aftereffects to abrupt splits in the treadmill belt speeds (Morton and Bastian, 2006). This is further supported by prior work that shows patients with cerebellar damage also do not adapt and store aftereffects to throwing with prisms (Martin et al., 1996), reaching with prisms (Weiner et al., 1983), an-

ticipatory catching (Lang and Bastian, 1999), postural standing (Horak and Diener, 1994), and force-field reaching (Gibo et al., 2013; Smith and Shadmehr, 2005).

Implications for walking rehabilitation

Given the likely connection between the cerebellum and sensory cancellation, we hypothesize that if this locomotor learning perception paradigm were tested with patients with cerebellar damage, we would not observe any changes in perception due to the fact that their cerebellum is not updating the expectations. We also predict that patients who suffer from schizophrenia may show deficits in this protocol as previous work has indicated that these patients show less sensory attenuation in a force-matching task (Shergill et al., 2014). In these patients, they have difficulty distinguishing between self and external sensory stimulation (resulting in hallucinations) which may indicate a disruption in the sensory-cancellation cerebellar circuit.

On the other hand, patients with cerebral stroke have been shown to be able to adapt to the split-belt training (Reisman et al., 2013, 2007, 2009). Following a short period of adaptation, patients show after-effects that temporarily reduce their step length asymmetry (Reisman et al., 2007). With repeated practice, these improvements tend to last for months after training (Reisman et al., 2013). However, perceptual learning in these patients has not be quantified, but anecdotal evidence suggests that some of these patients also show perceptual after-effects similar to those of controls (Reisman et al., 2007). Therefore, this suggests that we may be able to

use the split-belt treadmill to induce both motor and perceptual learning in these patients. It is possible by improving perception in these patients, they may be able to better detect their own gait abnormalities (Wutzke et al., 2015). Overall, the protocol implemented here may be a useful clinical tool for identifying and possibly reducing deficits for patients with neurological damage.

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Chapter 5

General conclusions

This doctoral work significantly contributes to the neuroscience and rehabilitation facets of biomedical engineering. Throughout all three projects in this thesis, we demonstrated that where people are placing their feet during walking gives us an insight into the neural mechanisms for locomotor adaptation. Adaptive learning is a powerful tool that shows great promise for gait rehabilitation. Therefore, the information learned from this doctoral thesis increases our understanding of human locomotor learning which lays the foundation for designing optimal rehabilitation strategies for patients with walking disorders.

Placing one foot in front of the other

Walking is a complex form of locomotion that requires coordination of multiple muscles across multiple joints. Nevertheless, we rarely think about how we are ac-

tually walking. In fact, when people are asked how they walk they may respond by saying "I place one foot in front of the other." While this response seems naive, we demonstrate in this thesis that it is not too far from the truth.

In this dissertation, we studied how people adapt their gait pattern while walking on a split-belt treadmill, with one belt moving faster than the other. Prior work has demonstrated that people adapt their walking pattern to minimize their step length asymmetry (Reisman et al., 2005). When the treadmill belts are returned to the same speed, subjects automatically limp for a while, indicating that they had learned a new gait pattern. While this prior work has suggested that the step length asymmetry represents an error signal, it was still unclear what particular aspect of the gait pattern was learned and then retained to minimize this error. In Chapter 2, we developed a descriptive model to decompose step lengths into spatial and temporal contributions. We showed that subjects changed both where and when they were placing their feet in order to cancel either an abrupt perturbation as shown in Chapter 2 or a gradual perturbation as shown in Chapter 3. Furthermore, we showed that when the belts were returned to the same speed the spatial contribution was retained and largely explained the after-effects in step length differences following learning. The temporal contributions did show after-effects, but they contributed very little to the overall step length difference after-effects. With respect to the observed step length difference after-effects, this indicates that while people are walking on the split-belt treadmill, they are learning where to place their feet.

In Chapter 3, we investigated how the addition of an explicit stepping strategy (monitored with a visual display in front of treadmill) influenced the after-effects of a gradual split-belt protocol. In these experiments, the explicit strategy was either congruent or incongruent with the adaptive learning. We observed that a congruent strategy neither enhances nor interferes with the after-effects. Interestingly, when the strategy was incongruent with adaptive learning (i.e. was used to interfere with natural adaptation pattern), we also observed no interference with the after-effects, suggesting that motor learning still occurs even if there are no behavioral changes during learning. This is similar to previous work in sequence learning which suggested that motor learning can still occur even if performance does not change (Seidler et al., 2005, 2002).

Where people are placing their feet also gives us insight into human locomotor perception. Prior work has demonstrated that following learning on the split-belt treadmill, subjects have recalibrated their perceptual system since they report that the previously slow belt is now faster when the belts are moving the same speed (Jensen et al., 1998; Vazquez et al., 2015). To investigate what mechanism is responsible for this, we designed a multi-phase experiment in Chapter 4 to measure their perception using psychophysical tasks. We utilized where people were placing their feet as an indicator of what treadmill speed was expected for each side of the body. Based on these expectations, we were able to predict their perceptual recalibrations in the psychophysical tasks using a sensory-cancellation mechanism, in which the ex-

pected sensory consequences of an action were cancelled from the incoming sensory signal. This result suggests that sensory cancellation is a commonly used mechanism in human perception since previous work in the human tactile system has also indicated use of the same mechanism (Blakemore et al., 1998).

Overall, these projects advance our understanding of how the healthy human locomotor system operates. This knowledge can be used for designing algorithms for artificial walking machines such as autonomous robots or exoskeletons. For example, machine learning algorithms focusing on foot placement can be used to help walking robots adapt their gait patterns when encountering new environments. Furthermore, it also suggests that artificial sensory systems may benefit from sensory cancellation.

Clinical implications

Not only does this research give us insight into human locomotion, but it also builds a foundation for gait rehabilitation. Over the last decade, there have been multiple studies (Reisman et al., 2013, 2007, 2009) investigating the effects of using split-belt walking for therapy with patients who have suffered a cerebral stroke. While the results are largely positive, it is still unknown why some patients improve and others do not. Given the findings about foot placement in this thesis, it is possible that the patients who improve may have had deficits in foot placement, since foot placement is generally retained after learning. On the other hand, this work suggests that an alternative technique should be considered for patients with temporal deficits

since their after-effects are small following split-belt walking. Future work should be conducted with these patients to test these hypotheses.

While split-belt walking produces positive rehabilitation outcomes, these treadmills are still very expensive and are not commonly available. As a result, other techniques must be pursued to have more immediate impact in many rehabilitation centers. One possibility known as unilateral stepping (Huynh et al., 2014; Kahn and Hornby, 2009) is to have patients put one foot on a fixed surface while walking with the other foot on a regular single-belt treadmill. However, results have shown that unilateral stepping produces less over ground transfer than split-belt walking (Huynh et al., 2014). We hypothesized that this difference was due to the lack of alternation between sides. Therefore, in Chapter 2, we had healthy subjects march with one foot on a stationary surface and walk with the other foot on a moving surface. Results indicated that subjects learned and retained new foot placements from this marching-walking hybrid in a similar manner to that of split-belt walking. It would be interesting to test this new technique with patients. We suspect that patients who are capable of bending their paretic knee (important for marching) would benefit from this behavior.

Conventional gait rehabilitation consists of having physical therapists instruct patients on how to move. This forces patients to explicitly think about how they are moving as they implement this new strategy. Nevertheless, there are multiple learning mechanisms that can be used for locomotor learning. In Chapter 3, we investigated

the effects of using explicit strategies simultaneously with adaptive learning. Interestingly, explicit strategies in isolation produced no immediate after-effects, whereas split-belt adaptation in isolation and with explicit strategies produced large immediate after-effects. This suggests that we should be designing rehabilitation strategies that utilize adaptive techniques.

Appendix A

Appendix for step length model

In this appendix, we derive a model for step length difference that separates the contributions from spatial, temporal and perturbation components. This derivation has been published elsewhere (Finley et al., 2015) but is provided here for clarity. We define step length as the anterior-posterior distance between the two ankle markers at heel strike. The fast step length occurs at heel strike on the fast treadmill belt and the slow step length occurs at heel strike on the slow treadmill belt. We define the step length difference as

$$Step\ Length\ Difference = Fast\ Step\ Length - Slow\ Step\ Length. \tag{A.1}$$

For a given stride, we define the first slow heel strike at time $SHS1$, the fast heel strike at time FHS and the second slow heel strike at time $SHS2$. We then define

the slow and fast step times (Malone et al., 2012), respectively, as

$$t_s = FHS - SHS1 \quad \text{and} \tag{A.2}$$

$$t_f = SHS2 - FHS. \tag{A.3}$$

For some time $TIME$, let $x_f(TIME)$ and $x_s(TIME)$ be the anterior-posterior position of the ankle markers for the fast and slow foot, respectively. These quantities are measured with respect to the average of the two hip markers to maintain a body-centered coordinate frame such that a positive value means the ankle is in front of the hip center (Finley et al., 2015). Using these variables, the step lengths are defined as

$$Fast\ Step\ Length = x_f(FHS) - x_s(FHS), \quad \text{and} \tag{A.4}$$

$$Slow\ Step\ Length = x_s(SHS2) - x_f(SHS2). \tag{A.5}$$

The approximate speed of each ankle (relative to the body) while on the moving belt can be written as v_s for the slow belt and v_f for the fast belt. We calculate these speeds with

$$v_s = \frac{x_s(SHS1) - x_s(FHS)}{t_s} \quad \text{and} \tag{A.6}$$

$$v_f = \frac{x_f(FHS) - x_f(SHS2)}{t_f}. \tag{A.7}$$

Given these definitions, we can rewrite the fast step length as

$$\begin{aligned} Fast\ Step\ Length &= x_f(FHS) - (x_s(SHS1) - v_s t_s) && \text{(A.8)} \\ &= \alpha_f + v_s t_s \quad \text{with} && \text{(A.9)} \\ \alpha_f &= x_f(FHS) - x_s(SHS1). && \text{(A.10)} \end{aligned}$$

As shown in Figure A.1, the fast step length is now decomposed into a spatial term α_f and a temporal term $v_s t_s$. The spatial variable only depends on where the two feet were placed relative to the body and the temporal variable depends on how far the slow foot moved backwards during the step time. Similarly, we can rewrite the slow step length as

$$\begin{aligned} Slow\ Step\ Length &= \alpha_s + v_f t_f \quad \text{with} && \text{(A.11)} \\ \alpha_s &= x_s(SHS2) - x_f(FHS). && \text{(A.12)} \end{aligned}$$

Note in Figure A.1, the spatial term α_s is drawn as negative indicating that the slow foot was placed behind the previous fast foot placement. We can now rewrite the step length difference equation as

$$Step\ Length\ Difference = (\alpha_f - \alpha_s) + v_s t_s - v_f t_f. \quad \text{(A.13)}$$

With some rearrangement, we can rewrite the step length difference as

$$Step\ Length\ Difference = \underbrace{(\alpha_f - \alpha_s)}_{Spatial} + \underbrace{\frac{v_s + v_f}{2}(t_s - t_f)}_{Temporal} + \underbrace{\frac{t_s + t_f}{2}(v_s - v_f)}_{Perturbation}. \quad \text{(A.14)}$$

This form of the step length difference equation is numerically equivalent to the difference in step lengths but breaks down the equation into spatial, temporal and perturbation contributions.

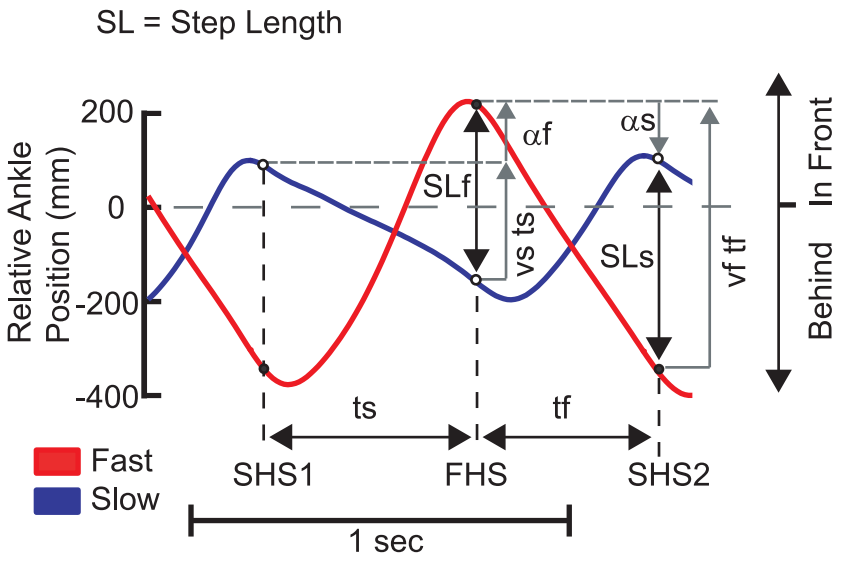

Figure A.1: Model Components Derivation. The ankle position relative to the hip center for the fast (red) and slow (blue) limbs is shown as a function of time. The step times t_s and t_f are the difference in times between heel strikes. Step length is defined as the distance between the two ankles as heel strike with the fast step length occurring with heel strike on the fast belt and slow step length occurring with heel strike on the slow belt. The spatial variables α_f and α_s represent the position of the heel strike relative to the previous heel strike. Note that α_s is drawn as negative since the slow foot is placed behind the fast foot.

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Vita

Andrew Long graduated *summa cum laude* from Northwestern University with a Bachelor of Science in Mechanical Engineering in 2009. Also in 2009, Andrew was awarded the Mechanical Engineering Undergraduate Academic Achievement Award for the highest cumulative grade point average and the Ovid W. Eshbach Award for overall excellence in scholarship and leadership. Andrew completed a Master's of Science in Mechanical Engineering at Northwestern University in 2011. His Master's thesis investigated dynamic locomotion of legged robotic systems. Andrew joined Dr. Amy Bastian's Motion Analysis Laboratory to pursue his Ph.D. in 2012. His research at Johns Hopkins University has focused on investigating human locomotor learning and its implications for rehabilitation.